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# SOUND OBJECTS IN TIME, SPACE AND ACTION

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# SOUND OBJECTS IN TIME, SPACE AND ACTION

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par

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# SOUND OBJECTS IN TIME, SPACE AND ACTION

The term “sound object” describes an auditory experience that is associated with an acoustic event produced by a sound source. At cortical level, sound objects are represented by temporo-spatial activity patterns within distributed neural networks. This investigation concerns temporal, spatial and action aspects as assessed in normal subjects using electrical imaging or measurement of motor activity induced by transcranial magnetic stimulation (TMS).

Hearing the same sound again has been shown to facilitate behavioral responses (repetition priming) and to modulate neural activity (repetition suppression). In natural settings the same source is often heard again and again, with variations in spectro-temporal and spatial characteristics. I have investigated how such repeats influence response times in a living vs. non-living categorization task and the associated spatio-temporal patterns of brain activity in humans. Dynamic analysis of distributed source estimations revealed differential sound object representations within the auditory cortex as a function of the temporal history of exposure to these objects. Often heard sounds are coded by a modulation in a bilateral network. Recently heard sounds, independently of the number of previous exposures, are coded by a modulation of a left-sided network.

With sound objects which carry spatial information, I have investigated how spatial aspects of the repeats influence neural representations. Dynamics analyses of distributed source estimations revealed an ultra rapid discrimination of sound objects which are characterized by spatial cues. This discrimination involved two temporo-spatially distinct cortical representations, one associated with position-independent and the other with position-linked representations within the auditory ventral/what stream.

Action-related sounds were shown to increase the excitability of motoneurons within the primary motor cortex, possibly via an input from the mirror neuron system. The role of motor representations remains unclear. I have investigated repetition priming-induced plasticity of the motor representations of action sounds with the measurement of motor activity induced by TMS pulses applied on the hand motor cortex. TMS delivered to the hand area within the primary motor cortex yielded larger magnetic evoked potentials (MEPs) while the subject was listening to sounds associated with manual than non-manual actions. Repetition suppression was observed at motoneuron level, since during a repeated exposure to the same manual action sound the MEPs were smaller. I discuss these results in terms of specialized neural network involved in sound processing, which is characterized by repetition-induced plasticity.

Thus, neural networks which underlie sound object representations are characterized by modulations which keep track of the temporal and spatial history of the sound and, in case of action related sounds, also of the way in which the sound is produced.

# LES OBJETS SONORES AU TRAVERS DU TEMPS, DE L'ESPACE ET DES ACTIONS

Le terme "objet sonore" décrit une expérience auditive associée avec un événement acoustique produit par une source sonore. Au niveau cortical, les objets sonores sont représentés par des patterns d'activités dans des réseaux neuronaux distribués. Ce travail traite les aspects temporels, spatiaux et liés aux actions, évalués à l'aide de l'imagerie électrique ou par des mesures de l'activité motrice induite par stimulation magnétique trans-crânienne (SMT) chez des sujets sains.

Entendre le même son de façon répétitive facilite la réponse comportementale (amorçage de répétition) et module l'activité neuronale (suppression liée à la répétition). Dans un cadre naturel, la même source est souvent entendue plusieurs fois, avec des variations spectro-temporelles et de ses caractéristiques spatiales. J'ai étudié la façon dont ces répétitions influencent le temps de réponse lors d'une tâche de catégorisation vivant vs. non-vivant, et les patterns d'activité cérébrale qui lui sont associés. Des analyses dynamiques d'estimations de sources ont révélé des représentations différenciées des objets sonores au niveau du cortex auditif en fonction de l'historique d'exposition à ces objets. Les sons souvent entendus sont codés par des modulations d'un réseau bilatéral. Les sons récemment entendus sont codé par des modulations d'un réseau du côté gauche, indépendamment du nombre d'expositions.

Avec des objets sonores véhiculant de l'information spatiale, j'ai étudié la façon dont les aspects spatiaux des sons répétés influencent les représentations neuronales. Des analyses dynamiques d'estimations de sources ont révélé une discrimination ultra rapide des objets sonores caractérisés par des indices spatiaux. Cette discrimination implique deux représentations corticales temporellement et spatialement distinctes, l'une associée à des représentations indépendantes de la position et l'autre à des représentations liées à la position. Ces représentations sont localisées dans la voie auditive ventrale du "quoi".

Des sons d'actions augmentent l'excitabilité des motoneurones dans le cortex moteur primaire, possiblement par une afférence du system des neurones miroir. Le rôle des représentations motrices des sons d'actions reste peu clair. J'ai étudié la plasticité des représentations motrices induites par l'amorçage de répétition à l'aide de mesures de potentiels moteurs évoqués (PMEs) induits par des pulsations de SMT sur le cortex moteur de la main. La SMT appliquée sur le cortex moteur primaire de la main produit de plus grands PMEs alors que les sujets écoutent des sons associée à des actions manuelles en comparaison avec des sons d'actions non manuelles. Une suppression liée à la répétition a été observée au niveau des motoneurones, étant donné que lors de l'exposition répétée au son de la même action manuelle les PMEs étaient plus petits. Ces résultats sont discuté en termes de réseaux neuronaux spécialisés impliqués dans le traitement des sons et caractérisés par de la plasticité induite par la répétition. Ainsi, les réseaux neuronaux qui sous-tendent les représentations des objets sonores sont caractérisés par des modulations qui gardent une trace de l'histoire temporelle et spatiale du son ainsi que de la manière dont le son a été produit, en cas de sons d'actions.

# LIST OF ABREVIATIONS

| | |
|---|---|
| AEP | auditory-evoked potential |
| BA | Brodmann area |
| BOLD | blood oxygen level dependent |
| ΔC | difference RP-IP within congruent sound pairs |
| ΔI | difference RP-IP within incongruent sound pairs |
| EEG | electro-encephalography |
| ELECTRA | electrical analysis |
| ERP | event related potential |
| EP | evoked potential |
| FDI | first dorsal interosseus |
| fMRI | functional magnetic resonance imaging |
| FS | first section |
| IID | interaural intensity difference |
| IP | initial presentation |
| LAURA | local autoregressive average |
| LS | last section |
| M+ | sounds related to manual actions |
| M- | sounds not related to manual actions |
| N1 | electrical negativity occurring at ca. 100ms post-stimulus onset |
| MEG | magneto-encephalography |
| MEP | motor evoked potential |
| N20m | magnetic negativity occurring at ca. 20ms post-stimulus onset |
| N50m | magnetic negativity occurring at ca. 50ms post-stimulus onset |
| PET | positron emission tomography |
| P2 | electrical positivity occurring at ca. 200ms post-stimulus onset |
| P2m | magnetic positivity occurring at ca. 200ms post-stimulus onset |
| RP | repeated presentation |
| s.e.m | standard error of the mean |
| SMAC | spherical model with anatomical constraints |

| | |
|---|---|
| TF | time frame |
| TMS | trancranial magnetic stimulation |

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# CHAPTER 1 INTRODUCTION

The processing of sound identity and location has been studied intensively over the last two decades in humans and non-human primates (Romanski et al., 1999; Kaas and Hackett, 1999; 2000; Rauschecker and Tian, 2000; Tian et al., 2001). Evidence favoring a dual-stream model for auditory processing of environmental sounds and speech has been accumulated with various techniques including anatomical (e.g. River and Clarke, 1997; Wallace et al., 2002) and activation studies (e.g. Maeder et al., 2001; Alain et al., 2004) in healthy volunteers, and neuropsychological investigation in brain damaged patient (Clarke et al., 2000; 2002). Broadly this model stipulates that information relative to the identity and the location of a sound source (often called the What and Where) are processed in parallel.

Regarding complex features of natural settings where subjects have to process sounds, little is known about the impact of the history of exposures to sounds and of positional information on cortical representations of the sound objects. An additional characteristic of natural settings is the fact that many sounds are the result of (manual) actions; listening to such sounds has been shown to co-activate motor and premotor cortices, arguing for auditory involvement in the mirror system.

I have investigated the cortical representations of sound objects using auditory evoked potentials (AEPs) and transcranial magnetic stimulation (TMS) and addressed three issues.

A. The modulation of temporo-spatial patterns of neural activity underlying sound object representations by the (temporal) history of exposure to these objects.

B. The coding of sound objects which carry spatial information, with specific interest in putative position-independent and position-linked representations.

C. The plasticity within the motor representation of action sounds.

## 1.1 Cortical representation of sound objects

### 1.1.1 Sound object

The term “sound object” is often used to describe an auditory experience that is associated with an acoustic event produced by a sound source (Griffiths and Warren, 2004; Nelken, 2004). In natural settings, a sound object provides information about its identity and its location. The former is processed along the ventral/”What” pathway through hierarchically organized levels of perceptual, semantic, and complex auditory scene analysis (Scott, 2005; Leaver and Rauschecker, 2010).

### 1.1.2 The dual stream model

Today’s view of auditory processing is very much influenced by the dual-pathway model (Arnott et al., 2004; Scott, 2005; Rauscheker and Tian, 2000; Rauschecker and Scott, 2009; Leaver and Rauschecker, 2010; van der Zwaag et al., 2011; see Fig.1). Evidence from electrophysiological studies from non-human primates (Tian and Rauschecker, 2004) as well as activation (Alain et al. 2001; Anourova et al., 2001; Arnott et al., 2004; De Santis et al. 2007; Lewis et al., 2004; Maeder et al. 2001) and lesion studies in humans (Clarke et al. 2000; 2002) points out a segregation between auditory processing which leads to sound recognition or to sound localisation. The separate processing within the ventral/What and the dorsal/Where streams offers the neural basis for the ultrarapid sound recognition (Murray et al. 2006), location-specific, rapidly occurring learning induced plasticity (Spierer et al. 2007) and specialised short-term memory systems (Kaiser et al., 2005).

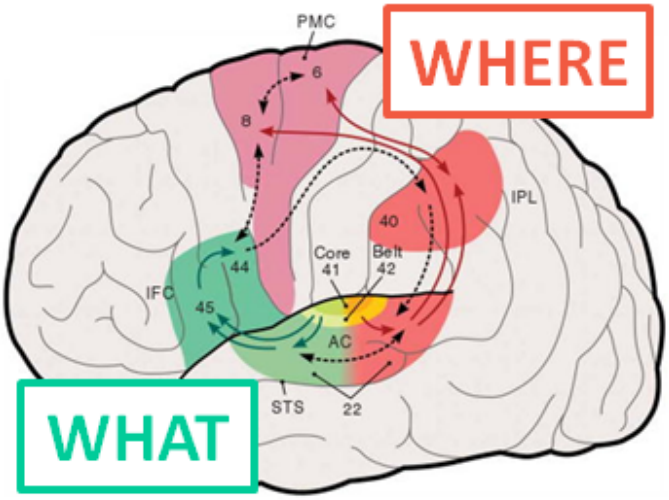


**Figure 1. The What and Where dual-stream model of auditory processing.**

At the cortical level the sound processing starts within the primary auditory area and then split into two streams: a ventral stream (in green) named the What stream as it is responsible for the processing of the identity of the sound object, and a dorsal stream (in red) named the Where stream as it is responsible for the processing of the localization of the sound object in the environment (adapted from Rauschecker and Scott, 2009).

### 1.1.3 Repetition priming as a way to explore object representation

Repetition priming refers to changes in the rapidity, accuracy or bias of processing a stimulus after a prior exposure to it and has been associated with a reduction in neural response (repetition suppression) or with an increase of neural activity (repetition enhancement) to the repeated stimulus, as compared to the first presentation of it (measured with fMRI or ERP). Repetition priming is defined as perceptual if it depends on the constancy of the physical features of the prime (initial stimulus) and target (repeated stimulus) and as conceptual if it depends on semantic proximity. Within a neuronal population repetition effects are believed to occur when the population encounters stimulus features which are perceived as identical. Three distinct mechanisms have been proposed to account for repetition suppression at neuronal level (for review see Wiggs and Martin 1998; Grill-Spector et al. 2006): i) "fatigue" within a neuronal population; ii) sharpening through a sparser neural representation; and iii) facilitation by synaptic potentiation (Fig.2).

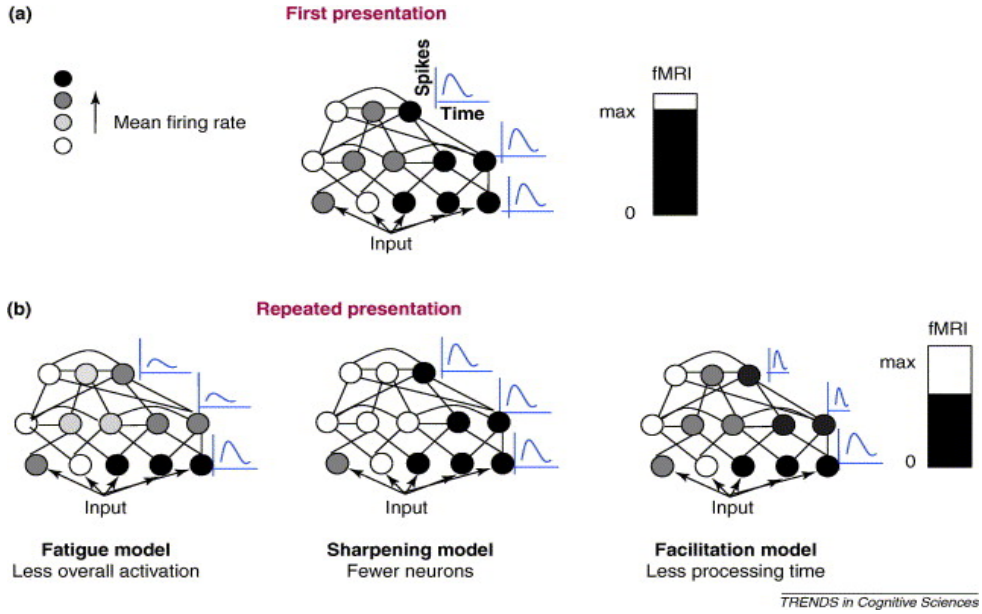


**Figure 2. Three distinct mechanisms for repetition suppression at neuronal level.**

(a) The stimulus causes activity in the input layer (corresponding to early sensory cortex) before being processed in a hierarchical sequence of stages. (b) The three patterns of neuronal activity for the repeated stimulus as postulated by the three models: the Fatigue model (left, lower firing rates); the Sharpening model (centre, fewer neurons responding); and the Facilitation model (right, shorter duration of neural processing). The blue graphs indicate spiking of the neurons as a function of time. The highest response at each stage is indicated by black circles (adapted from Grill-Spector et al., 2006).

Repetition priming had been extensively used as a tool to explore object representations in the visual domain (for reviews see e. g. Henson et al. 2003; Grill-Spector et al. 2006). In the auditory domain perceptual and/or semantic priming with environmental sounds has shown decreases in neural activity along the ventral/What pathway, including the non-primary auditory areas (Bergerbest et al., 2004; Doehrmann et al., 2008; Altmann et al., 2010) and the temporal convexity (De Lucia et al., 2010b), at ca. 150-220ms post-stimulus onset (Murray et al., 2008a) or at P2m (Altmann et al., 2008).

## 1.2 Representation of the temporal history of exposure to sound objects

### 1.2.1 Repetition priming for environmental sounds

As mentioned before, repetition priming using environmental sounds improves stimulus recognition (Chiu and Schacter, 1995; Stuart and Jones, 1995; Chiu, 2000) and decreases neural activity in specific regions along the ventral auditory pathway, including the non-primary auditory areas (Bergerbest et al., 2004; Altmann et al., 2010) and the temporal convexity (De Lucia et al., 2010b). Electrophysiological studies identified the critical time window for repetition suppression at 156-215ms post-stimulus onset (Murray et al., 2008a or at P2m Altmann et al., 2008). Interestingly, the recent history of exposure to the same sound is coded at a later stage than the initial sound object categorization, which starts as soon as 70-100ms post-stimulus onset (Murray et al., 2006; De Lucia et al., 2010a; see Fig.3).

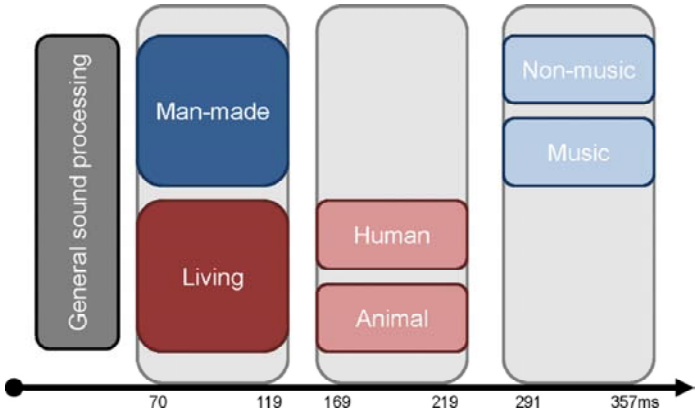


**Figure 3. Schematic representation of a temporal hierarchy in auditory object discrimination.**

In a hierarchical fashion over time, general sound processing (initial 70 ms) is followed by living versus man-made discrimination (70 –119 ms), then by human versus animal vocalization discrimination (169 –219 ms), and finally by the discrimination of musical instruments versus other man-made objects (291–357 ms), (adapted from De Lucia et al., 2010a).

### 1.2.2 Number of stimulus exposures

Small numbers of repetitions of the same (visual) stimuli have been found to modulate behavioral priming (Wiggs and Martin, 1998) and to progressively increase repetition suppression. In animals, response suppression at the neural level continued to decrease with

repeated presentations, but this decrease became smaller across successive repetitions as stimuli became familiar (Li et al., 1993). In functional magnetic resonance imaging (fMRI) experiments, activations tended to decrease monotonically with the number of repetitions, often reaching a plateau after 6 to 8 repetitions (Henson et al., 2000; Grill-Spector and Malach, 2001; Sayres and Grill-Spector, 2006). Multiple repetitions, as carried out in priming paradigms, were proposed to contribute to lasting changes at different levels of cognitive representations (Schacter et al., 2004) and to play a role in the induction of long-term memory (Hauptmann and Karni, 2002). Thus, repetition paradigms are likely to help to unravel the neural underpinning of explicit and implicit learning, which may offer new tools for rehabilitation of brain-damaged patients. The effect of multiple repetitions has not been explored in the auditory modality. Furthermore, it is not known whether the adaptation through multiple repetitions allows the brain to keep nonetheless track of recent repetitions among the multiple presentations.

Further, relatively little is known about how multiple repetition suppression influences the perceptual and semantic level representations within the auditory "What" pathway. Repetition suppression following one or few repetitions has been repeatedly demonstrated using acoustically identical environmental sounds in fMRI (Bergerbest et al., 2004) or magnetoencephalography and electroencephalography. In a recent fMRI study perceptual and semantic contributions to repetition priming of environmental sounds have been shown to yield similar behavioral effects and similar suppression within the ventral/"What" pathway, suggestive of similar mechanisms for both (De Lucia et al., 2010b). None of the studies so far has investigated the brain plasticity following numerous repetitions of sound object.

## 1.3 Representation of sound objects in space

### 1.3.1 Ecological relevance of combined semantic and spatial representation of sound sources

In natural settings, sounds arise from various sources of distinct and possibly moving locations. When we hear a bird singing for the second time, it may no longer be on the same branch as the first time. Having a full understanding of the surrounding environment implies binding auditory semantic and spatial information provided by the same source (e. g. the bird) into a common concept.

### 1.3.2 How do the streams interact?

Our everyday experience gives us a convincing demonstration of unified perception of the identity of a sound object and its location and raises the question of how and at what level the two streams interact. The seminal study which demonstrated an early separation between the What and Where streams within non-human primate early-stage auditory areas, has also clearly documented the existence of a subpopulation of neurons, which has a combined selectivity for semantic (monkey calls) and spatial information (Tian et al., 2001; for What and Where segregation at early-stage non-primary auditory areas in cat see Lomber and Malhotra, 2008). A recent 7T activation study suggested that this is also the case in human ea*rly-stage areas*; in one of two early-stage areas, which have been previously shown to be selective for sound recognition (as compared to sound localization; Viceic et al., 2006), responses to environmental sounds were shown to be modulated by spatial information (van der Zwaag et al., 2011; see Fig.4).

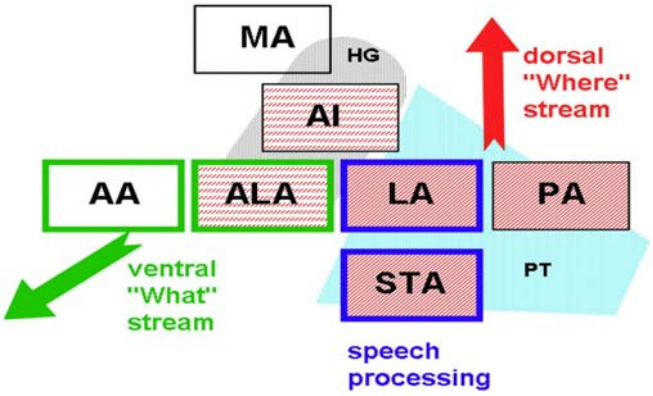


**Figure 4. What and Where pathways within the early auditory areas.**

The early-stage auditory areas have been identified on the basis of architectonic criteria (Rivier and Clarke, 1997; Wallace et al., 2002). Comparison with activation studies revealed a specialization for sound recognition in AA and ALA (Viceic et al., 2006), and for speech processing in LA and STA (Scott and Johnsrude, 2003) Within the ventral/What stream position-linked (ALA) and position-independent (AA) representation of environmental sounds have been described (Van der Zwaag et al., 2011). AA: anterior area, ALA: anterolateral area, AI: Primary auditory area, MA: medial area, LA: lateral area, STA: superior temporal area, PA: posterior area, HG: Heschl's gyrus, PT: planum temporal (adapted from Van der Zwaag et al., 2011).

It is currently unclear, whether within higher-order auditory cortices, and in particular along the auditory What and Where streams, a same neural network carries representations for combined specific semantic and spatial information. I have addressed this issue using the repetition priming paradigm, while searching for position-independent and position-linked representations of sound objects. I use here the term “sound object” as previously defined to describe an auditory experience that is associated with an acoustic event produced by a sound source (Griffiths and Warren, 2004; Nelken, 2004); so it refers to both living and non-living sound sources and has, in natural settings, a semantic and a spatial dimension.

So far none of the studies have investigated repetition priming effects linked to the spatial attributes of sound objects. Environmental sounds used for repetition priming experiments were presented without spatial cues in acoustically identical or different exemplars (Chiu & Schacter, 1995; Chiu, 2000; Ojemann et al., 2001; Schweinberger, 2001; Bergerbest et al., 2004; De Lucia et al., 2009). In everyday life, however, the location of the sound object in

respect to the listener is subject to changes, because the sound object or the listener are likely to move.

## 1.4 Representations of action sounds

Apart from the well documented activations within auditory regions, action-related verbal (Pulvermüller, 1999; Pulvermüller et al., 2001; Pulvermüller et al., 2003; Hauk et al., 2004; Pulvermüller, 2005; Tettamanti et al., 2005; Pulvermüller and Fadiga, 2010) and environmental sounds (Lewis et al., 2005; Pizzamiglio et al., 2005; Gazzola et al., 2006; Hauk et al., 2006; Lahav et al., 2007; De Lucia et al., 2009; Giusti et al., 2010) were shown to co-activate parts of prefrontal, premotor and motor cortices. Within the motor cortex TMS and fMRI studies revealed a somatotopy associated with listening to speech; thus action words such as “lick”, “pick” and “kick” co-activated the mouth, hand and foot representations within the motor areas (Hauk et al., 2004; Pulvermüller et al. 2005).

The demonstration of auditory-motor representations of words and more generally the role of the parieto-frontal circuits in auditory verbal comprehension lead to the reconsideration of the relationship between sensory and motor circuits in auditory verbal perception and comprehension (Hickok and Poeppel, 2007; Pulvermüller and Fadiga, 2010). Modular models which have been influential over many decades consider that motor activation during stimulus processing is due to feedforward projections after extensive processing within sensory cortices and has thus no crucial function in perception or comprehension (Hubel, 1995; Fodor, 1983; and Shallice, 1988 quoted by Pulvermüller and Fadiga, 2010); they posit that perception and action are supported by separate processing components. Pulvermüller and Fadiga, (2010) argue in their recent review for a distributed action-perception model of auditory verbal comprehension (or more generally beyond the language: Rizzolatti et al., 2001) on the basis of several observations. The discovery of mirror neurons (Fig.5) in the non-human primate cortex (Rizzolatti et al., 1996) is a strong argument in favor of the integration of motor circuits in perception, especially in the speech/language domain.

Macaque area F5, where mirror neurons have been repeatedly recorded, is cytoarchitectonically similar to Brodmann area 44 and is hence believed to be a putative homologue of Broca's area; (Rizzolatti and Arbib, 1998). The involvement of Broca's area in auditory verbal perception is further supported by neuropsychological studies demonstrating comprehension impairments in Broca's aphasia (e.g. when patients are tested with speeded up speech or in noisy environment; Moineau et al., 2005). Furthermore, the recognition of specific phonemes activated brain region specifically involved in the production of those speech sounds (Wilson et al., 2004; Pulvermüller et al., 2006; D'Ausilio et al., 2009).

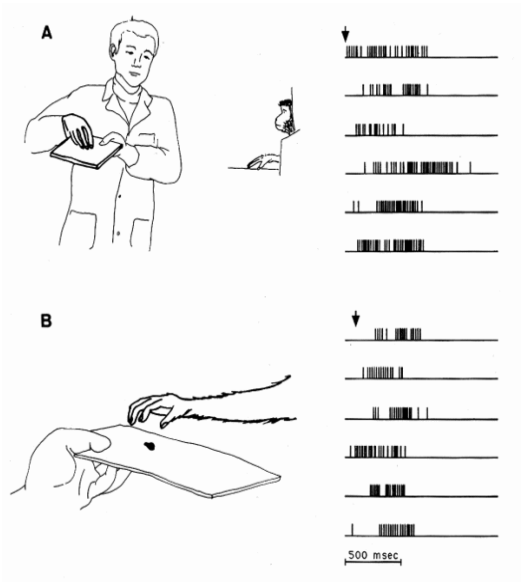


**Figure 5. Mirror neurons in non-human primate**

A mirror neuron discharges when the monkey is observing a person performing an action (a grasp movement; A) and when the monkey is performing the action itself (B). So, mirror neurons code for the action regardless of who is performing it, the person or the monkey itself. The patterns of discharge of the mirror neurons are displayed on the right (adapted from Rizzolatti and Fabbri Destro, 2008).

Moreover, apraxic patients also exhibited difficulties in (visual) recognition of actions, indeed, hand and mouth action-related sound recognition are specifically impaired in limb and buccofacial apraxic patients, respectively (Pazzaglia et al., 2008).

Auditory-motor representation has been also demonstrated for non-verbal sounds within the motor cortex. Lewis et al., (2005) reported evoked activity for tool sounds mostly in the left hemisphere including the middle portion of the left inferior frontal sulcus, the left ventral premotor cortex, in addition to several parietal and temporal sites. Gazzola et al., (2006) reported activation within the left BA44, BA6, and within parietal and temporal regions both when subjects listened to actions and when they executed them. In addition, Lahav et al., (2007) showed bilateral activations in the frontoparietal motor-related network (Broca, premotor, intraparietal sulcus, inferior parietal region) for listening to trained music compare to untrained musics. Doehrmann et al., (2008) showed specific brain activity for tool sounds in the left postcentral gyrus/insula, middle frontal gyrus, as well as bilateral temporal and parietal regions. Further, De Lucia et al., (2009) studied sounds that eliciting actions from the listener (when we hear a ringing phone we shall answer it) and found a higher activity for sound eliciting actions within the bilateral premotor and the left inferior prefrontal regions.

Listening to sounds elicited by action was shown to coactivate (Hauk et al., 2006) or increase the excitability of the corresponding motor cortex (Aziz-Zadeh et al., 2004); and listening to sounds that in everyday life cue for actions (e.g. to pick up a phone that is ringing) co-activated premotor and inferior prefrontal regions (De Lucia et al., 2009). The link between action sounds and motor neurons has been demonstrated by transcranial magnetic stimulations (TMS) of the hand representation within the primary motor cortex; the magnetic evoked potentials (MEPs) within the first dorsal interosseus muscle (FDI) were larger when the subjects listened to action related environmental sounds (typing and tearing paper sound) than non-hand related sounds (Aziz-Zadeh et al., 2004).

It is currently not clear whether motor representations of environmental sounds are part of the semantic representations within the auditory ventral/What stream or whether they constitute a functionally distinct, “ready-for-action” system. Repetition priming, which is believed to occur when a neuronal population repeatedly encounters stimulus features which it perceives as identical, is often used to explore neural representations of objects (for reviews see e.g. Henson, 2003; Grill-Spector et al., 2006).

Listening to repeated environmental sounds yielded response suppression in non-primary auditory areas (fMRI; Bergerbest et al., 2004) and beyond them on the left middle temporal gyrus and superior temporal sulcus (EEG; Doehrmann et al., 2008; Altmann et al., 2008; Murray et al., 2008a). Comparing repetition suppression due to priming by semantically-but-not-acoustically identical environmental sounds to that by acoustically identical sounds revealed that repetition suppression was characteristic of the semantic representation within the ventral/ What pathway (fMRI; De Lucia et al., 2010b). In a task using visual verbal primes and auditory non-verbal targets, repetition suppression associated with action-related sounds was found within the left superior temporal and premotor cortices (whereas suppression associated with non-action sounds was limited to temporal cortex; Pizzamiglio et al., 2005). The motor representation of action sounds has not yet been assessed through a repetition priming paradigm.

In an animal model of aplysia motor responses can be shaped by the network state or by the input or a combination of both. Increase of firing rate has been reported with stimulation repetitions (Friedman et al., 2009; Friedman and Weiss, 2010.).

## 1.5 Learning and memory

Memory is the ability to encode, maintain and recall information; it comprises rather heterogeneous aspects (Augustine et al., 2011) that can be described regarding time (short-term vs. long-term memory) and type of information (declarative memory vs. non-declarative memory). The declarative memory represents all the knowledge that can be reported verbally or graphically under conscious recall and is assessed by explicit tasks (e.g. What was the words I asked you to memorize? What was the name of your first teacher?). The declarative memory can be divided into two main distinctions: the episodic memory and the semantic memory. The episodic memory corresponds to memory processing of unique events; this kind of knowledge comprises information about the time and the location of its acquisition (e.g. the memory of the last holiday or the last birthday party or a list of words). This type of memory

depends critically on the integrity of the middle temporal lobe, more specifically with the hippocampal formation (Augustine et al., 2011, for amnesic patient study see Corkin et al., 1997). The semantic memory is independent of the recall of the context of its acquisition (e.g. one's own name and address or the vocabulary of a language). The non-declarative memory does not require conscious recall and is assessed by implicit tasks (i.e. identification of degraded pictures that have been previously seen or to perform a motor task that has been previously trained). The non-declarative memory can be divided into perceptual and procedural memory. The perceptual memory represents the ability to process more efficiently the already stored information. The procedural memory involves cognitive and motor skills required to perform a task.

Learning is the processing whereby information is encoded to be maintained in memory. An important aspect of the learning process is the repetitions of the information. Notably for the non-declarative memory Hauptmann and Karni (2002) argued that the saturation of priming effect occurring after several repetitions is crucial for the induction of long-term memory.

## 1.6 Hypotheses

I studied the impact of the (temporal) history of exposure to sound objects on their representations at the cortical level. Generally speaking, repetitions represent the basics of learning. The number of repetitions as well as the time lag to the last exposure is crucial even for passive and/or implicit learning. I hypothesized that these parameters also influence the cortical representations of sound objects.

I have investigated repetition priming effects of lateralized environmental sounds using an auditory evoked potential paradigm. The analysis was driven by the hypothesis that the human auditory cortex carries both position-independent and position-linked representations of sound objects. The former were expected to be characterized by priming effects which are

independent of the respective lateralizations of the prime and repeat, while the latter yield priming effects only when the semantic information and lateralization coincide.

I tested the hypothesis that co-activation of the primary motor cortex is a part of the semantic representation of action sounds and that this activation shares key features. In particular, I predicted that repeated exposure to the same sound object will yield repetition suppression and not repetition enhancement, which characterizes neural networks subserving ready-to-go motor systems (Friedman et al., 2009; and Friedman and Weiss, 2010). MEPs of the FDI muscle were evoked by single pulse TMS to the hand area in the primary motor area and their modulation by manual-action-related or –unrelated environmental sounds evaluated in a repetition priming paradigm.

### 1.6.1 Hypothesis on the impact of the temporal history of exposure to sound objects on their cortical representations (Study A)

A recent, single exposure to a sound object and a repeated, frequent exposure to it modulate in a different way the temporal-spatial patterns of neural activity that underlie sound recognition.

### 1.6.2 Hypothesis on the coding of sound objects which carry spatial information (Study B)

A sound object which carries positional information activates, at the cortical level, both a position-independent and a position-linked representation. These representations can be revealed by repetition priming paradigms.

### 1.6.3 Hypothesis on the plasticity of the motor representations of action sounds (Study C)

The motor representations of action sounds share the priming-induced plasticity with the semantic representations within the ventral/What stream.

# CHAPTER 2 MATERIALS AND METHODS

The current work concerns neural plasticity of the semantic representation of environmental sounds and can be divided into three studies. The first study (A) focuses on the effect of single vs. multiple repetitions over time and addresses the question of the impact of the temporal history of exposure to sound objects on their cortical representations. The second study (B) assesses the coding of sound objects which carry spatial information with a particular stress on the spatially dependent representations versus the spatially independent representations of auditory objects. The third study (C) concerns the involvement of motor cortical networks in the processing of sounds related to manual actions. More precisely, I studied the plasticity of the representations of actions. These three studies are likely to lead to three distinct publications (Bourquin et al., a, b, c in preparation).

The two first studies (A and B) had been carried out using electrical neuroimaging methods on the same data set (but addressing different questions and presenting different analysis contrasts). The third study (C) had been conducted with transcranial magnetic stimulation associated with motor evoked responses of a hand muscle (i.e. the first dorsal interosseus).

## 2.1 Studies A and B:
## Impact of the temporal history of exposure to sound objects on their cortical representations
## Coding of sound objects which carry spatial information

### 2.1.1 Participants

Twelve right-handed men (mean ± SD lateralization index = 84.08 ± 6.30; Oldfield, 1971) aged between 20-38 years (mean ± SD = 26.3 ± 5.5 years) participated in the study. None had

history of neurological or psychiatric illness, and all reported normal hearing. Participants provided written informed consent and were remunerated modestly for their participation in this study. This study was approved by the Ethics Committee of the Faculty of Biology and Medicine at the University of Lausanne.

### 2.1.2 The experimental procedure

I investigated neural plasticity associated with repetition priming of environmental sounds with particular emphasis on characteristics of the repeats, which are likely to occur in natural settings. To ensure ethologically relevant conditions, sound objects were presented many times, at different positions and repeats consisted of a mixture of semantically identical but acoustically different stimuli or of acoustically identical stimuli. Indeed, we often hear sounds numerous times e.g. along a road we likely would hear car motors again and again. Regarding the spatial location of these repetitions, it is noteworthy that car sounds will arise from both sides of the road i.e. spatial changes will occur within the sound exposures.

More precisely, participants completed a total of 16 blocks (B1-B16), each of which comprised two presentations of 40 meaningful and easily identifiable environmental sounds. The sounds were 500ms in duration, including a 50ms linear raise and fall time; (16 bit stereo; 22.5kHz digitization) and were normalized according to the root mean square of their amplitude. Half of the sounds referred to living human and non-human vocalizations (baby crying, bird, cat, coughing, chicken, clearing throat, cow, crow, dog, donkey, frog, gargling, laughter, owl, pig, rooster, scream, sheep, sneezing, and whistling), and the other half to man-made sound sources (accordion, bicycle bell, car horn, cash register, church bell, cuckoo clock, doorbell, door closing, flute, glass shattering, guitar, harmonica, harp, organ, piano, police siren, saxophone, telephone, trumpet and violin; as already used by Murray et al., 2006). The task was a two-alternative forced choice in which participants had to classify as rapidly and as accurately as possible each sound as living or man-made by pressing one of two buttons of a serial response box using the index and middle finger of the right hand.

Within each of the 16 blocks, sounds were presented with a pseudo-random inter-stimulus interval of 1600ms to 2400ms (in 100ms steps). The initial and the repeated presentations of a

given sound object were either acoustically different (exemplars a-b, b-a) or identical (a-a, b-b) the four possibilities accounted each for 25% of the pairs within a block and were pseudo-randomly distributed across the 16 blocks of the whole experiment (see Fig.6).

The stimuli were delivered with an interaural intensity difference of 53dB ± 3dB favoring the left (L) or right (R) ear through insert earphones (ER-4P; www.etymotic.com) at a sound pressure level of 88dB ± 3dB for the leading ear (measured with a CESVA SC-L sound pressure meter; cesva.com). The spatial lateralizations of the initial and the repeated presentations of a given object within a block were either the same or different (R-R, L-L, R-L, L-R; the 4 possibilities accounted each for 25% of the pairs within a block and were mixed pseudo-randomly). The relationship between the acoustic nature of the repeated exemplar (identical or not) and its position with respect to the initial presentation (same or different) was pseudo-randomized and balanced across sound objects and subjects. The blocks were separated by six minute breaks, during which the participants were exposed to another kind of auditory stimuli (series of four pure tones) which were irrelevant to the experimental paradigm of both the multiple repetition and spatial priming studies. In addition, the time lag between repetitions and the number of intervening items was kept constant across participants and ranged from 2 to 12 sec. (0 to 5 distinct intervening items, none of them were exemplars of the same auditory object) for the within block presentation. Regarding the between blocks repetition, the temporal interval between the exposure to a specific sound object ranged from ca. 6 to 8min (0 to 38 items, none of them were exemplars of the same auditory object). Finally, in order to avoid systematic bias arising from order presentation across subjects, the presentation order of the blocks was determined by a Latin square design. The whole experiment lasted approximately 2.2 hours.

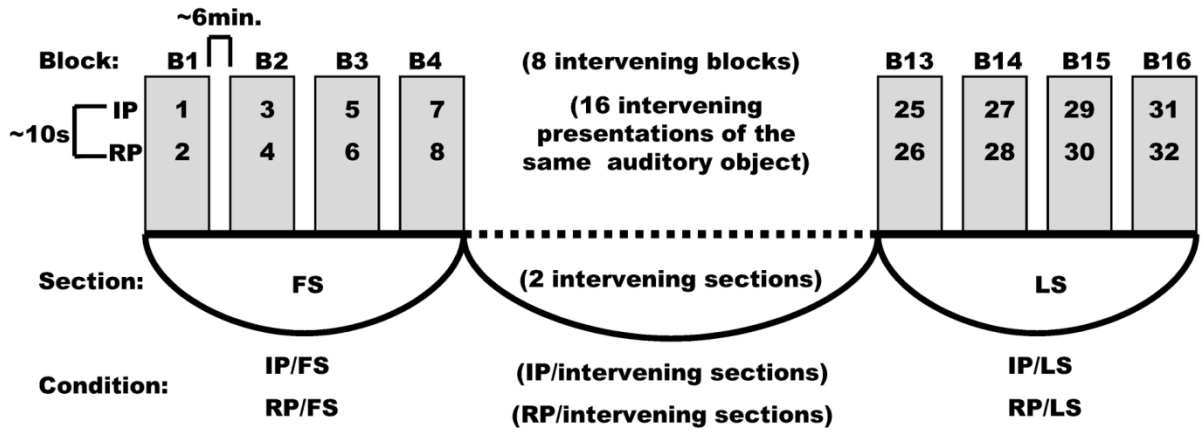


**Figure 6. Schematic representation of the experimental paradigm.**

Sixteen blocks (B1 – B16) of 80 stimuli each (50% living, 50% man-made) were grouped into 4 sections (FS-LS) of 4 blocks each for the purpose of study A. Within each block the same sound source had an initial (IP) and a repeated (RP) presentation that correspond to the factor of presentation and are used in both studies A and B. Within a section the same number of congruent and incongruent pairs was presented. The four experimental conditions used in study A are displayed: initial (IP) vs. repeated (RP) presentations within the first (FS) and the last (LS) section. Thus, the data from the first and the last section were used in Study A, while the data from the whole experiment were used in Study B.

### 2.1.3 Analyses of temporo-spatial pattern of neural activity associated with the impact of the temporal history of exposure to sound object (study A)

The multiple repetitions study aimed at comparing the behavioral and electrophysiological effects of few vs. numerous repetitions of auditory objects. The analysis of auditory evoked potentials included the comparison of primes vs. repeats (effect of presentation) and that of the first quarter vs. the last quarter of the experiment (effect of section). Thus, I used a 2 X 2 within-subject experimental design with factors of presentation (within block initial vs. repeated presentation; hereafter IP and RP, respectively) and section (first section vs. last section; hereafter FS and LS, respectively) (see Fig.6).

### 2.1.4 Analyses of temporo-spatial pattern of neural activity associated with the coding of sound objects which carry spatial information (study B)

Study B aimed at comparing the electrophysiological difference of sound processing arising from the initial and the repeated presentations (hereafter IP and RP, respectively) of the sound

within congruent sound pairs vs. incongruent sound pairs (C vs. I, respectively). More precisely, I contrasted the congruent priming (i.e. priming occurring within spatially congruent presentations: L-L or R-R pairs; C/RP-C/IP: hereafter ΔC) with the incongruent priming (i.e. priming occurring across spatially incongruent presentations: L-R or R-L pairs; I/RP-I/IP: hereafter ΔI). Thus, the analysis of auditory evoked potentials included the comparison of the difference: repeats minus primes within congruent pairs vs. incongruent pairs (effect of congruency on priming: sounds from spatially congruent pairs vs. sounds from spatially incongruent (opposite) pairs; ΔC and ΔI, respectively). These analyses were conducted with the data from the whole experiment regardless of the section.

Moreover, in order to assess common parts of the spatially congruent and incongruent priming I contrasted initial vs. repeated presentations of sounds regardless of the congruency (factor of presentation: within block initial vs. repeated presentation; IP and RP, respectively). This analysis corresponds to the factor of presentation from Study A, however, for Study B I used the data from all the sections of the experiment (and not only the first and the last sections), thus I will have more statistical power.

### 2.1.5 Electroencephalography (EEG) analysis approach

In order to study the spatio-temporal brain dynamics during sound perception we employed event-related potentials (ERPs) based on electroencephalographic (EEG) recordings. The ERP analysis approach employed assumes that brain activity is trigged by the automatic processing of a stimulus (such as a sound) in a time-locked manner to the onset of the event. This characteristic is a prerequisite for the averaging of the electrical signal across stimulus presentations in order to increase the signal-to-noise ratio. By doing so, EEG signal averages aim at emphasizing the part of the signal that represents the brain response to a certain stimulus, i.e. the ERP or EP (evoked potential). Please note that in the current work concerned with sound processing (cf. in particular the studies on multiple repetitions and spatial priming), the notion of auditory evoked potentials (AEPs) is used as a synonym to ERPs.

The head surface EEG recordings utilized for data collection have the advantage to be noninvasive as electrode sensors are placed at the scalp of the volunteers. These electrodes

continuously record the ongoing electrical signals generated by the brain, in particular ionic currents due to neural, mainly postsynaptic, activity. In contrast to invasive (single cell) EEG recordings, head surface EEG can only capture the synchronous activity of parallel neuron populations (mainly pyramidal neurons). Only the parallel organization of pyramidal neurons creates a so-called open electric field configuration allowing for the summation of electrical signals by synchronous neuronal discharges, in turn creating an electric field that can be measured at the scalp surface (as opposed to a non-parallel neuron organization and closed electric field properties).

### **2.1.6** The EEG acquisition

For the two EEG studies (A and B) presented here the EEG data acquisition had been obtained as follows. Continuous EEG was recorded at 1024Hz through a 160 channel Biosemi ActiveTwo system (Biosemi, Amsterdam, Netherlands). EEG pre-processing and analyses were performed using Cartool (Brunet et al., 2011). EEG epochs including 100ms pre- to 500ms post-stimulus onset were averaged, and auditory evoked potentials (AEPs) were calculated for the various experimental conditions (i.e. the four conditions of study A: IP/FS, RP/FS, IP/LS, and RP/LS, as well as the four conditions of study B: ΔC, ΔI, IP, RP). Trials with eye blinks or transient noise were rejected offline using a semi-automated ± 60μV criterion at every channel. The average number of accepted epochs per condition was 141 ± 2 (mean ± s.e.m.) for study A and there was no significant difference in the number of accepted trials across the experimental conditions ($F_{(3,9)}<1.92$, $p>0.20$). In study B, the average number of accepted epochs per condition (C/IP, C/RP, I/IP, and I/RP) was 268.6 ± 1.7 (mean ± standard deviation), and 537.2 ± 3.8 for the IP and RP conditions. Again, there was no significant difference in the number of accepted trials across the experimental conditions ($F_{(3,9)}<0.21$, $p=0.89$, and $T_{(11)}<0.81$, $p=0.43$, respectively). Prior to group averaging, data at artifact channels from each subject were interpolated using 3-dimensional splines (Perrin et al., 1987). Data were then recalculated against the average reference and band-pass filtered between 0.68 and 40Hz. Data were baseline corrected over the 100ms pre-stimulus period during group-averaging.

### 2.1.7 The analyses of the Auditory evoked potentials (AEPs)

As a first level of analysis, I performed time point-wise within-subject analyses on the AEP waveforms from each of the electrodes. For study A, I used a 2 X 2 repeated measures ANOVA with factors presentation (IP vs. RP) and section (FS vs. LS). For study B, I used a paired t-test with the factor of presentation (IP vs. RP) as well as a paired t-test with the factor of congruency (ΔC vs. ΔI). Correction was made for temporal autocorrelation at an individual electrode level (Guthrie and Buchwald, 1991) through the application of a > 20 consecutive time frames (i.e. ~20ms at 1024Hz digitization) criterion for the persistence of significant effects. No overt correction for spatial correlation was made.

### 2.1.8 The intracranial source estimations

Different electrical neuroimaging methods are currently used for the investigation of intracranial sources at the origin of the recorded EEG signal at the scalp. Innovative source estimation methods have been developed and used in basic and clinical research over the last years Michel et al., (2004); Murray et al., (2008b); Brunet at al., (2011). Post-stimulus time intervals for which neural source differences can be expected are therein often defined by time periods of interest over which topographic modulations across experimental conditions are observed in the scalp-surface ERPs. According to physical properties of electric fields, changes in surface electric field topographies are forcibly accompanied by changes in the underlying neural generators (Lehmann, 1987).

However, topographic analyses on scalp-surface ERPs operate on data that is normalized for response strength. That is, when differences between experimental conditions consist of ERP amplitude modulations that are not accompanied by topographic changes, underlying differences in neural source activation strength would be neglected. In other words, if an identical network of brain regions is activated by varying experimental conditions, a topographic analysis of surface ERP responses would gain no consistent results. However, at the same time it cannot be concluded that the neural sources underlying the ERPs for each condition do not differ in terms of activation strength or intensity, respectively.

Functional neuroimaging studies on repetition priming often show a reduction in the neural activity within similar brain networks underlying initial and repeated stimulus representation (Henson, 2003; Grill-Spector et al., 2006). In line with these findings, our attempts to find global modulations in the surface ERP topographies between experimental conditions did not yield conclusive results, i.e. we were not able to define a time period of interest for neural source estimations based on surface topographic ERP differences.

In order to be nevertheless able to analyze differences in neural source activity between conditions, we utilized an approach (by courtesy of J.-F Knebel) to compare neural source strength millisecond- and node-wise across the full post-stimulus epoch. By doing so, time periods of activation differences between conditions could further be obtained in an observer- and reference-independent way.

I estimated the sources in the brain underlying the AEPs recorded using a distributed linear inverse solution (ELECTRA), applying a local autoregressive average (LAURA) regularization approach (Grave de Peralta et al., 2001; Grave-de Peralta et al., 2004; Michel et al., 2004). LAURA selects the source configuration which best mimics the biophysical behavior of electric vector fields (i.e. activity at one point depends on the activity at neighboring points according to electromagnetic laws: potentials decay as a function of the square distance to the source). LAURA uses a realistic head model; the solution space includes 3005 nodes, selected from a 6 × 6 × 6 mm grid equally distributed within the gray matter of the Montreal Neurological Institute average brain. The head model and lead field matrix were generated with the Spherical Model with Anatomical Constraints (SMAC; Spinelli et al., 2000). As an output, LAURA provides current density measures; the scalar values of which were evaluated at each node. Prior work has documented and discussed in detail the spatial accuracy of this inverse solution (e.g. Grave de Peralta Menendez et al., 2004; Gonzalez Andino et al., 2005a; Gonzalez Andino et al., 2005b; Brodbeck et al., 2009; Groening et al., 2009; Martuzzi et al., 2009; Vulliemoz et al., 2009).

Source estimations were calculated for each time frame (TF), each experimental condition and each subject. Then, only for study A, the data were down-sampled from 1024Hz to 512Hz in

order to reduce the number of statistical tests. The data were corrected based on the maximum of the pre-stimulus activity, i.e. the scalar value of each solution point at each TF post-stimulus onset was reset to zero when it was below the highest scalar value reached during the 100ms pre stimulus onset period at the corresponding solution point. This procedure reduces contamination of the source estimations and the related statistical effect by ghost source activity, before the statistical analyses. The corrected scalar value of the activity at each solution point and for each time frame were submitted to the same procedure as for the waveform analysis (i.e. time point-wise 2 x 2 repeated measures ANOVA with factors presentation (initial vs. repeated presentation) and section (first vs. last section) for study A; and time point-wise paired t-tests with factors of presentation and congruency for study B; see Ortigue et al., 2005; Plomp et al., 2010; Britz and Michel, 2010; Knebel et al., 2011). To reduce the risk of false positive results arising from multiple tests within study A, I used a node-wise significance threshold of p-value < 0.01, a temporal criterion of >15 consecutive TFs (~29ms), and a spatial criterion of 8 contiguous solution points for significant effects. A p-value < 0.01 and/or other criteria allow to be more restrictive, as required because of multiple testing, and avoid the problem of being too strict with Bonferroni corrections (Genovese et al., 2002). In other words, I first selected among the 769280 ANOVAs (i.e. the activity of 3005 node scalar values X 256 TFs), those resulting in a p-value of maximally 0.01. Then, the number of positive results was reduced according to the temporal criterion, so that only effects occurring at a specific location for at least 15 consecutive TFs were retained. Finally, the spatial criterion was applied so that among the remaining positive results, only those belonging to a cluster of at least eight contiguous solution points, at each time frame, were retained. Regarding study B, I used slightly different criteria for significant effects: a node-wise significance threshold of p-value < 0.05, in addition to a temporal criterion of >18 consecutive TFs (~18ms), and a spatial criterion of 15 contiguous solution points (see Gutherie and Buchwald, 1991 for a discussion of threshold criterion).

## 2.2 Study C:
## Plasticity of the motor representations of action sounds

The third study (C) was conducted with rather different methods than the two previous studies. I investigated sound representations related to the motor circuit by applying transcranial magnetic stimulation (TMS) in combination to the recording of motor evoked responses in a hand muscle. Basically, a change of the electrical field induces a magnetic field which in turn is at the origin of an electrical field modulation. Thus, applying TMS single pulses over a brain region will transiently change its neuronal activity. The use of a figure-of-eight coil allows obtaining a change of the neuronal activity over a rather focal cortical region. When applied over the motor cortex of the hand TMS single pulses can induce motor evoked responses (MEPs) in the contralateral hand muscles. Thus, TMS single pulses associated with MEP recordings can be used as a tool for assessing the motor circuit.

### 2.2.1 Participants

Eighteen right-handed (mean ± SD = 89.17 ± 14.58; Oldfield, 1971) volunteers (12 females) aged between 19-26 years (mean ± SD = 23.2 ± 2.3 years) participated in the study. Thirteen were amateur musician (playing from 1 to 5 musical instruments for a period of 3 to 12 years, thus, the majority of them has more precise motor representations of how to play musical instruments than non-musicians), none had history of neurological or psychiatric illness, and all reported normal hearing. Participants provided written informed consent and were moderately remunerated for their participation. All procedures were approved by the Ethics Committee of the Faculty of Biology and Medicine at the University of Lausanne.

### 2.2.2 The experimental procedure

The stimuli were 60 environmental sounds of which 30 were related to manual actions (M+) and 30 were not (M-). The category M+ included 10 sounds related to unimanual (clinking glasses; brushing; hooting; knocking on a door; filling up a glass with a liquid; leafing through a book; spraying; dialing a phone number; ringing a bicycle bell; slapping), 10 to bimanual (playing the accordion, harp, piano, violin, drum, tambourine; typing; using the pneumatic drill; clapping hands; sharpening a knife), and 10 to hand-face actions (playing the

recorder, flute, bagpipes, trumpet; brushing teeth; coughing; Native American war cry; whistling; hissing; shaving). The category M- included 10 sounds related to face (snoring; crying baby; and saying: [o], [di], [ʒy], [la], [ni], [vɑ], [ga], and [ʒi]), and 10 to leg actions (running; tap dancing; steps on different floor material: two types of gravel, flagstone, tiled floor, two types of wooden floor, resonant courtyard, and two kind of street steps), while 10 were unrelated to immediate human action (a plane; cricket; helicopter; clock; storm; hens; wind; dog; train; fire). These sounds were 4s in duration, including a 50ms linear raise and fall time; (16 bit stereo; 22.5kHz digitization) and were normalized according to the root mean square of their amplitude. They were presented at an intensity of 80 ±3dB through insert earphones (ER-4P; www.etymotic.com). Each sound was followed by a 3s silent interval (Fig.7). Before the TMS experiment, subjects heard the 60 sounds and classified them as belonging to one of the six subgroups by pressing on a button. This was done to allow the participants to become familiar with the task, notably with the six sound categories. The use of these six sound categories helped the volunteers to reach a precise representation of the action sounds. The TMS experiment comprised 4 experimental blocks consisting of 60 trials each; during the first two blocks TMS was delivered to one hemisphere and during the last two blocks TMS was delivered to the other hemisphere (i. e., a prime block and a repeated block of sounds associated with the stimulation of each hemisphere). The order of stimulated hemisphere was counterbalanced across subjects.

During TMS to the hand representation within the right hemisphere MEPs from the left FDI muscles were recorded and vice-versa (Fig.7). Recording electrodes were mounted on the belly of the FDI (after cleaning with abrasive gel and alcohol); ground and reference electrodes (unipolar montage) were placed on the left upper arm for the recordings of the left hand signal and on the right upper arm for the recordings of the right hand signal (as in Aziz-Zadeh et al., 2004). During recording the hand was positioned on the arm rest of the Magstim chair. Digitization sampling rate was 1000Hz. Single trancranial magnetic pulses (Magstim Rapid2 Transcranial Magnetic Stimulator, Magstim Company, Spring Gardens, UK) were delivered by an eight-figure coil to the hand representation within the primary motor cortex at random 2.0; 2.25; 2.5; 2.75; or 3.0 s post-stimulus onset. The hand area was identified for each subject as the optimal site to elicit motor hand response (as in Aziz-Zadeh et al., 2004; Théoret et al., 2004). The motor threshold was determined as the minimal intensity which induced MEPs >50μV peak-to-peak amplitude in at least 5 out of 10 trials (as in Aziz-Zadeh

et al., 2004; Fecteau et al., 2005). For MEP recordings, single-pulse TMS was delivered at 120% of the motor threshold of the subject and hemisphere.

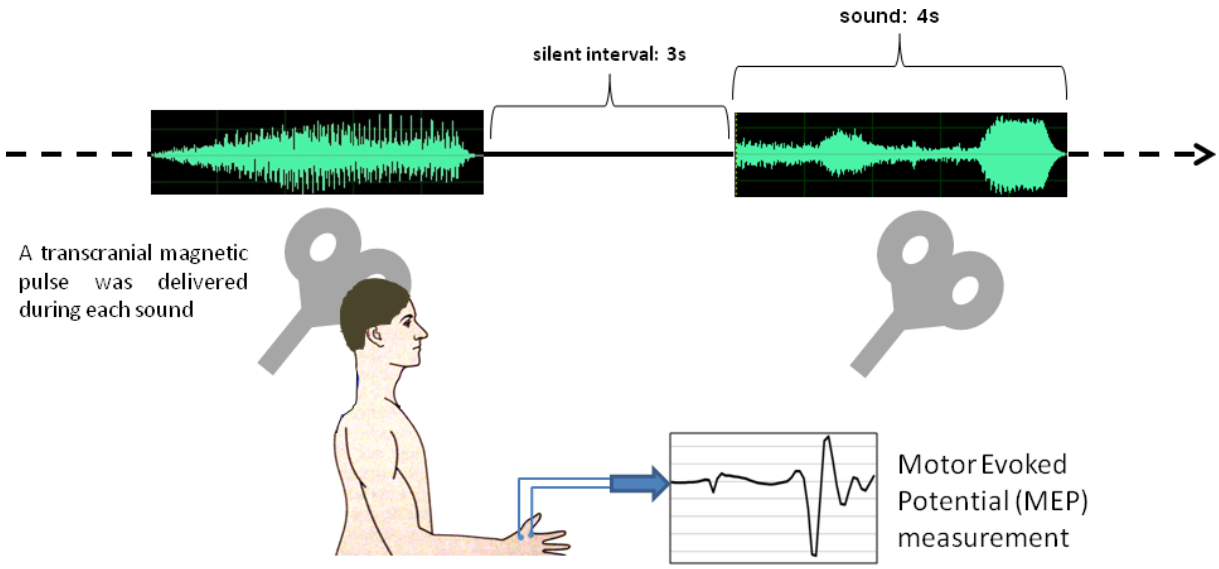


**Figure 7. Paradigm.**

Example of stimulation of the left hemisphere and the recording of the motor evoked response from the right hand. The sound duration was 4s and the interval between the sounds was 3s. During the presentation of each sound a transcranial magnetic pulse was delivered to the hand motor cortex and the motor evoked potential induced by the pulse was recorded from the contralateral hand.

### 2.2.3 Signal processing

For each subject, MEPs were averaged over the -100 to 200ms period trigged by the TMS pulses separately for the data from each hand. Data were band-pass filtered between 0.3 and 500Hz (with 50Hz notch filter) and baseline corrected over the 100ms pre-stimulus period during group-averaging. The MEPs were then averaged for each subject with respect of the experimental block (factor of presentation: initial vs. repeated presentation) and the sound category (factor category: M+ vs. M-). For each subject the peak-to-peak amplitudes of MEPs of each experimental condition were normalized in respect to the mean MEP of all categories (and are hence indicated in percentage of it), separately for the right and the left FDI.

Recordings with higher modulations occurring before the TMS pulse compared to after were eliminated. The MEPs of one hand were incomputable for three subjects and these data were then discarded.

### 2.2.4 Analyses of motor evoked potentials associated with the plasticity of the representations of action

Normalized MEPs from the right and left hand were analyzed separately using a 2x2 within subject repeated measures ANOVA with the factors category of sounds (M+ vs. M-) and presentation (initial vs. repeated).

As the aim of this study was to assess the plasticity of the representation of action sounds, I analyzed the repetition effect and I chose the general sound category contrast (i.e. M+ vs. M-) as the second factor to have enough trials per condition. Nevertheless, even if I cannot analyze the effect of the repetitions for the six sound categories, the analysis of the six sound categories regardless of the repetitions would be of great interest and will likely be analyzed separately further.

Moreover, I chose to conduct two separated 2x2 within subject ANOVA, one for the data associated with the stimulation of the left hemisphere and one for the data associated with the stimulation of the right hemisphere rather than a three ways ANOVA with the factor of hemisphere to be stimulated. Indeed this three ways ANOVA was discarded for several reasons. First this will have reduced the power of the analyses as the data associated with the stimulation of one hemisphere had to be rejected due to poor signal to noise ratio for some participants while the data collected when stimulating the other hemisphere were retained. Second, the signal recorded at the muscle of the left hand was referenced to a different electrode than the signal recorded at the right hand. Moreover, the electrode placements on the muscle of the left and right hand may be slightly different introducing additional variations in the signal that were not associated with a studied factor.

# CHAPTER 3 RESULTS

## 3.1 Impact of the temporal history of exposure to sound objects on their cortical representations (study A)

The aim of this study was to investigate the impact of the temporal history of exposure to sound objects on their cortical representations. More specifically, I hypothesized that a recent, single exposure to a sound object and a repeated, frequent exposure to it modulate in a different way the temporal-spatial patterns of neural activity that underlie sound recognition.

### 3.1.1 Behavioral level

All subjects readily categorized all stimuli as living vs. man-made (mean accuracy ± s.e.m: 95% ± 0.02% correct responses) and tended to be more rapid with repetition. The response times to the initial (IP) and repeated presentation (RP) in the first (FS) and the last section (LS) were analyzed with a 2 x 2 repeated measure ANOVA with factors presentation and section (mean response time ± s.e.m: IP/FS: 715.7 ±25.3ms, RP/FS: 692.7 ± 24.0ms, IP/LS: 664.5 ± 22.8ms, and RP/LS: 655.5 ± 21.4ms; see Fig.8). There was a significant main effect of factor presentation ($F_{(1,11)}$=12.44; $p<0.05$) and a marginally significant effect of section ($F_{(1,11)}$=4.29; p=0.06). There was no significant interaction between these factors ($F_{(1,11)}$=3.06; p=0.11). Thus, the response time for sound categorization decreased significantly when the same sound source was repeated 2-12 sec. later within the same block. Furthermore, there was a tendency for shorter response times in the last as compared to the first section. This result provides one level of argument against a simple explanation in terms of fatigue.

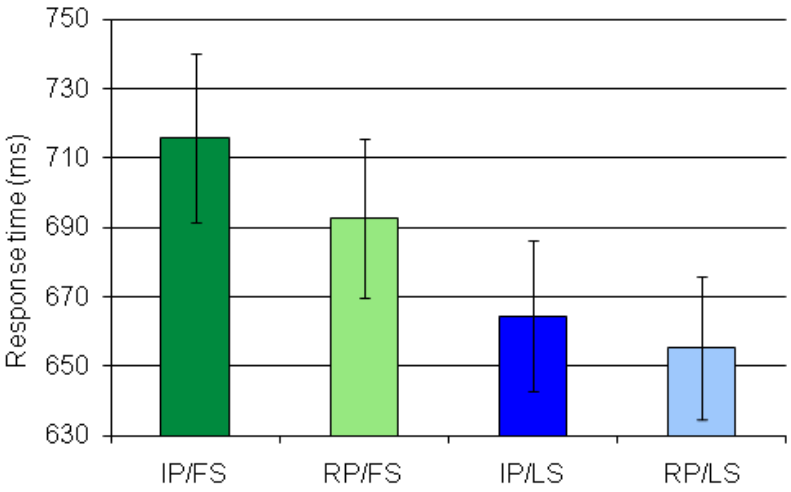


**Figure 8. Response time.**

Mean response time for the four conditions (error bars: s.e.m): IP: initial presentation, RP: repeated presentation, FS: first section, LS: last section. There is a decrease of response time over the repetitions.

### 3.1.2 Electrode level

The AEPs recorded at the individual electrodes showed a significant effect of presentation, section and/or interaction of both at different time frames, in particular over the N1-P2 complex (example of electrode Fz in Fig.9).

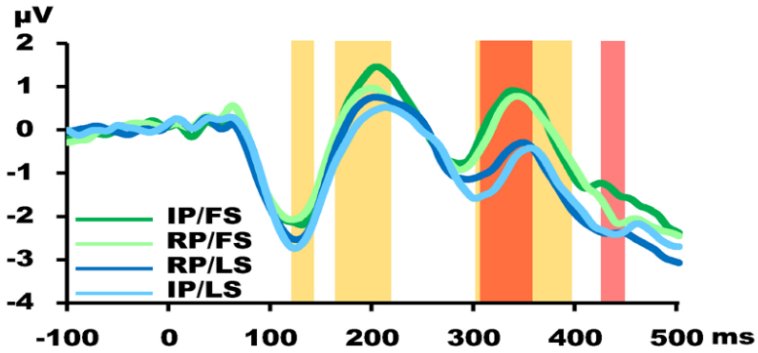


**Figure 9. AEP modulations.**

The potentials measured at a frontal midline site were significant ($p<0.05$) for the factor of presentation at 300-450ms post-stimulus onset period (in red), for factor section at 100-200ms and 300-400ms post-stimulus onset periods (in yellow); there was no interaction.

### 3.1.3 Brain space level

The time frame-wise 2 X 2 repeated measures ANOVA with factors of presentation (initial, repeated presentation) and section (first, last section) performed on source estimations was applied to all solution points (periods of significant modulations are shown in Fig.10). This analysis revealed a cluster of solution points exhibiting a significant main effect of presentation and two distinct clusters of solution points exhibiting a significant main effect of section (Fig. 11). There was no evidence for clusters exhibiting a significant interaction between these factors.

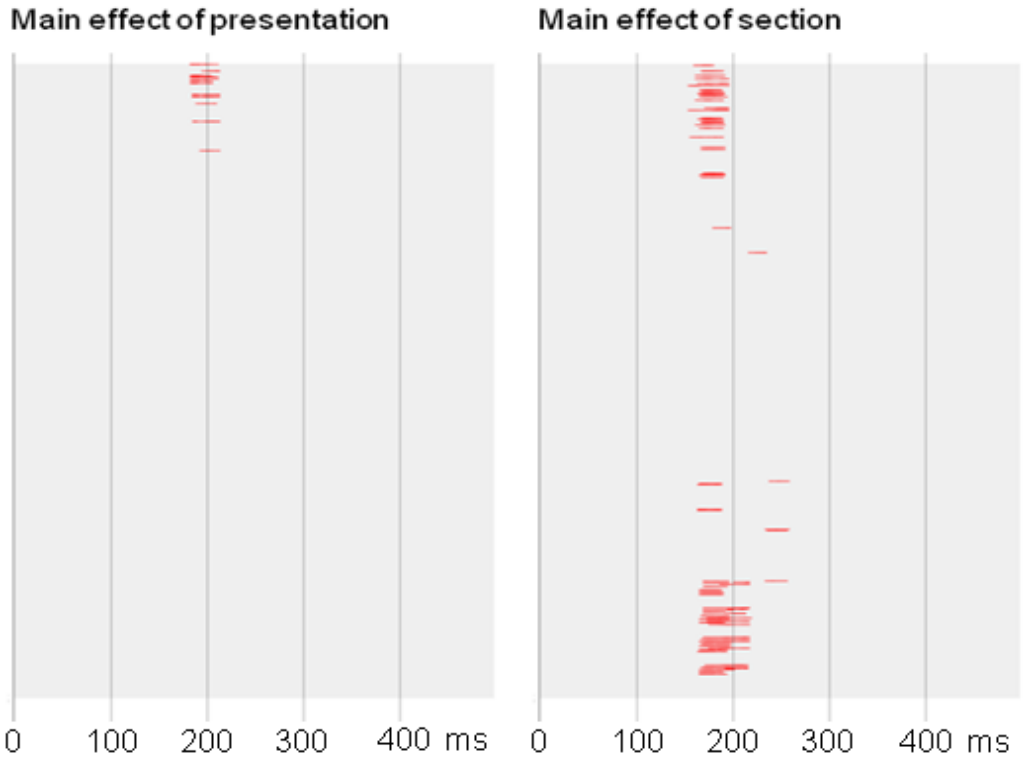


**Figure 10. Significant modulations of all solution points across time.**

The left panel represents the significant modulations (in red) of all the solution points across time for the main effect of presentation. The right panel represents the significant modulations (in red) of all the solution points across time for the main effect of section. (No significant modulations were found for the interaction between the two factors). The 3005 solution points are displayed vertically.

### *3.1.3.a Priming effect for recently heard objects*

A significant main effect of presentation was present over the 182-215ms post-stimulus onset period in a cluster including the left temporal convexity (planum temporale, superior and middle temporal gyri; Fig.11; Talairach and Tournoux, 1988). This effect was driven by significantly stronger activity during the initial presentation than the repeated presentation of the sound, irrespective of section.

### *3.1.3.b Priming effect for often heard objects*

A significant main effect of section was found in two clusters; one included the left temporoparietal convexity (planum temporale, superior and middle temporal gyrus, supramarginal gyrus, angular gyrus) and occurred over the 152-199ms post-stimulus onset period (Fig.11; Talairach and Tournoux, 1988). This effect was driven by significantly stronger activity within the first section than the last section of the experiment. This cluster included the location with significant effect of presentation described above. The other cluster included the right temporo-parieto-frontal cortex (pre and postcentral gyrus, planum temporale, superior and middle temporal gyrus, superior and inferior parietal lobules, and the insula), where the significant main effect of section occurred over the 162-221ms post-stimulus onset period (Fig.11). This effect was driven by significantly stronger activity within the first section than the last section of the experiment.

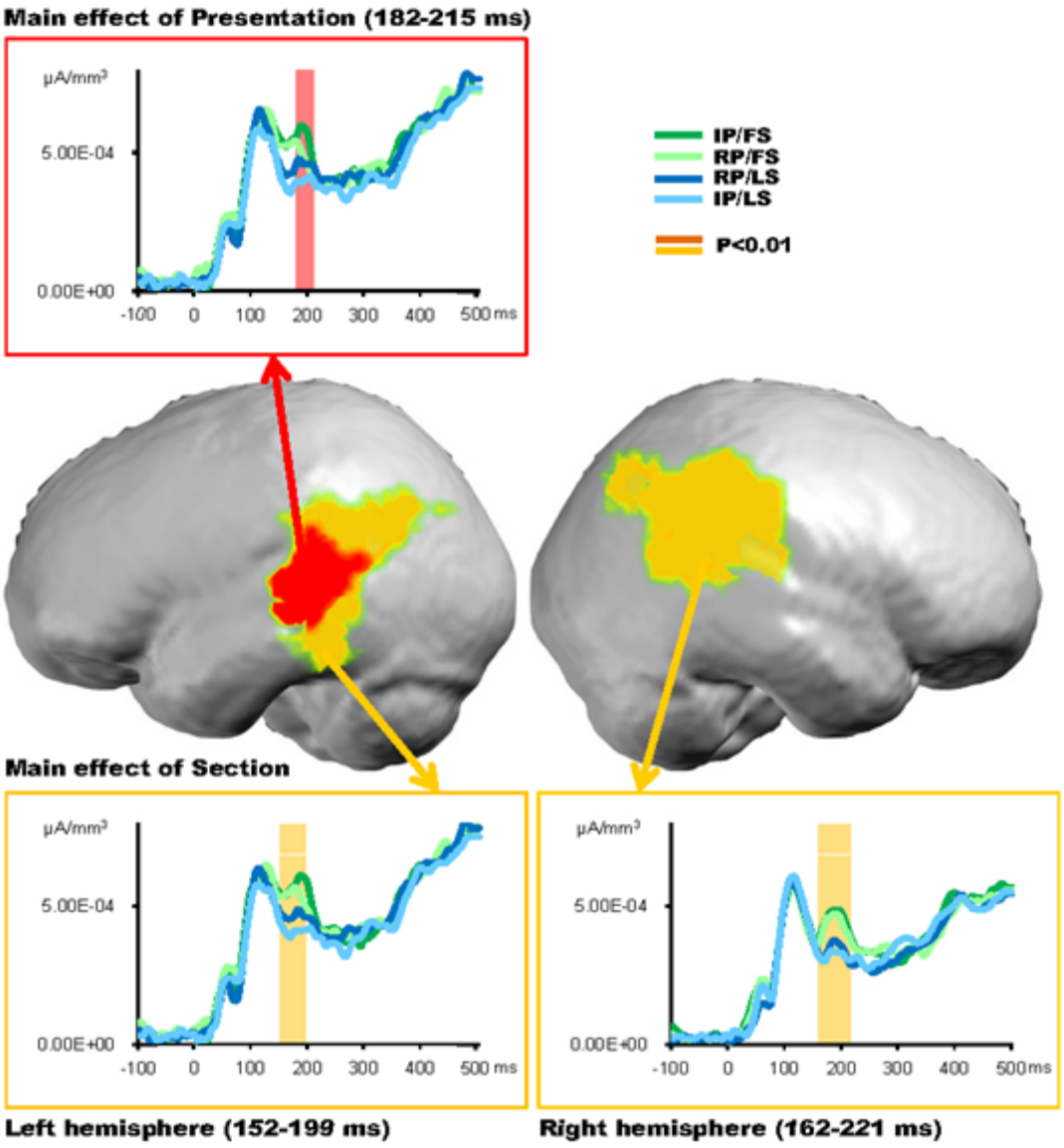


**Figure 11. Inverse solution modulations.**

Significant modulations as a factor of presentation occurred within a cluster (in red) including the left temporal convexity (superior and middle temporal gyrus) and the insula occurring over the 182-215ms post-stimulus onset period. The significant modulations as a factor of section implied two clusters (in yellow). The first cluster included the left temporo-parietal convexity (planum temporale, superior and middle temporal gyrus, supramarginal gyrus, angular gyrus) and the significant effect occurred over the 152-199ms post-stimulus onset period. The second cluster included the right temporo-parietofrontal cortex (planum temporale, pre and postcentral gyri, superior and middle temporal gyrus, superior and inferior parietal lobules, and the insula), the significant effect occurred over the 162-221ms post-stimulus onset period.

## 3.2 Coding of sound objects which carry spatial information (study B)

The aim of this study was to investigate the impact coding of sound object carrying spatial information. More specifically, I hypothesized that a sound object which carries positional information activates, at the cortical level, both a position-independent and a position-linked representation. I explored these representations with a repetition priming paradigm.

### 3.2.1 Behavioral level

All subjects readily categorized all stimuli as living vs. man-made (mean accuracy ± s.e.m: 95% ± 0.02% correct responses). The response times to all initial (IP) and all repeated presentation (RP) were not significantly different (mean response time ± s.e.m: 732.5 ± 3.4ms vs. 727.2 ± 3.5ms, respectively; paired t-test; $T_{(11)}$=1.05; $p$=0.32). In addition, the difference in response times to the initial (IP) and repeated presentation (RP) of sounds from congruent (C) and incongruent pairs (I) were analyzed with a paired t-test with factor of congruency (ΔC vs. ΔI) to disentangle possible effects of congruency on priming (see Fig.12). Indeed, there was a significant main effect of factor of congruency on priming (defined as the subtraction of IP from RP; $T_{(11)}$=-2.56; $p$<0.05); I observed repetition priming effect within congruent pairs (mean response time ± s.e.m: 12.5 ±5.2ms; $T_{(11)}$=-2.26; $p$<0.05) but not within incongruent pairs (mean response time ± s.e.m: -1.9 ±6.0ms; $T_{(11)}$= 0.32; $p$=0.75). Thus, the response time for sound categorization decreased significantly when the same sound source was repeated on the same side whereas this was not the case when the repetition occurs on the opposite side.

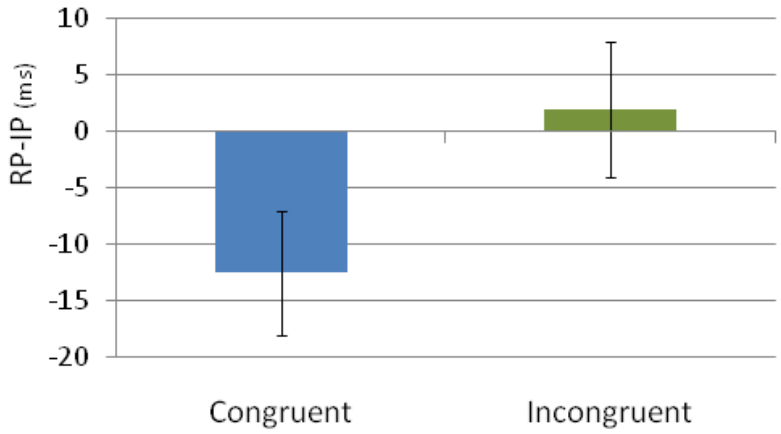


**Figure 12. Difference of response time RP-IP.**

The mean difference of response time (RP-IP in ms) of the congruent pairs differs from the difference of response time of the incongruent pairs (error bars: s.e.m). There is a facilitation of repetition for the congruent pairs, but not for the incongruent pairs.

### 3.2.2 Electrode level

The AEPs recorded at the individual electrodes showed a significant effect of congruency as well as effect of presentation at different time frames. Time frame-wise paired t-tests performed on the whole electrode montage revealed significant modulations of the factor congruency at left fronto-temporo-parietal sites mainly over the 20-50ms post-stimulus onset period, as well as more widespread effects over the and 410-470ms post-stimulus period. Significant modulations of the factor presentation occurred at frontal, occipital and left temporo-parietal sites over the 130-220ms (revealing a modulation of the auditory N1-P2 complex), as well as more widespread effects over the 320-460ms post-stimulus period.

### 3.2.3 Brian space level

#### *3.2.3.a Priming effect in congruently vs. incongruently lateralized repetition pairs*

Temporo-spatial patterns of neural activity associated with position-linked representations of sound objects were identified by differences in priming effects (repeats minus primes) yielded by congruent vs. incongruent pairs (hereafter ΔC and ΔI, respectively). The time frame-wise

paired t-tests with factor of congruency performed on source estimations were applied to all solution points (similar procedure as for study A). The analysis revealed two distinct clusters of solution points exhibiting a significant effect of congruency (Fig.13).

Over the 20-39ms post-stimulus onset period, a left temporal cluster comprising the posterior parts of the superior and middle temporal gyri (but not the planum temporal) yielded repetition suppression for congruent and repetition enhancement for incongruent pairs. Posthoc analysis revealed that during this time window the repetition suppression in congruent pairs and the repetition enhancement in incongruent pairs were statistically significant. Indeed, the mean activity of the cluster was statistically different from zero over the 22-40ms and over the 24-39ms post-stimulus onset periods for the congruent vs. incongruent condition, respectively (see Fig.14).

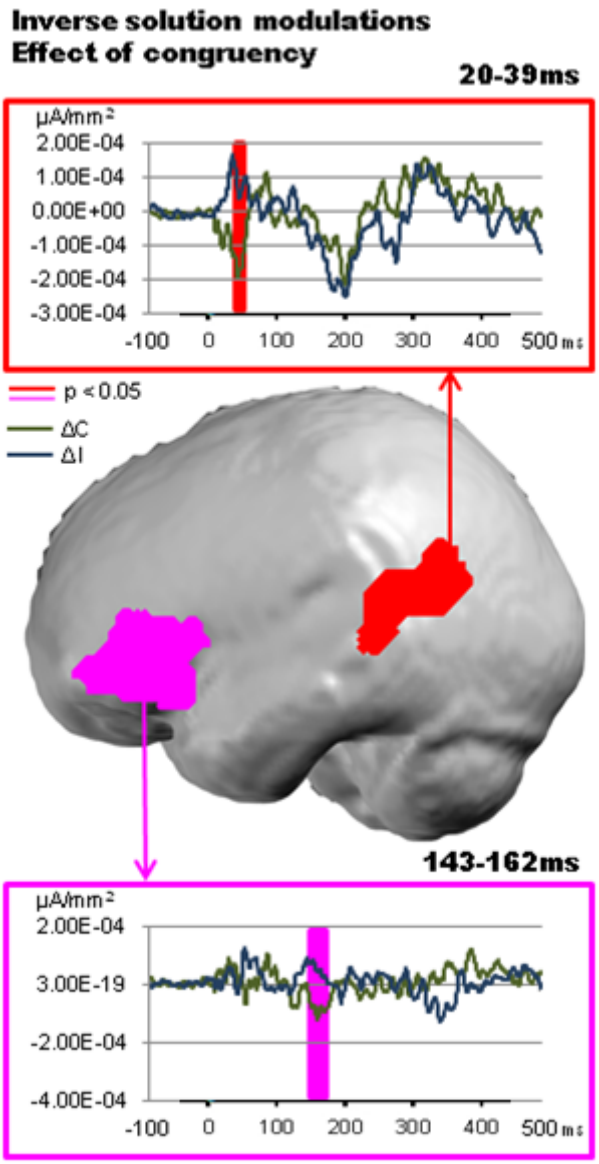


**Figure 13. Inverse solution modulations. Effect of congruency.**

The left temporal brain region (the red cluster), as well as the frontal brain region (the pink cluster), exhibited significant differences across priming within spatially congruent vs. incongruent pairs (ΔC vs. ΔI). The priming modulations of the congruent pairs are represented in green and the priming modulations of the incongruent pairs are represented in blue (top panel for the red cluster, lower panel for the pink cluster). The red and the pink bars represent the period of significant differences. The modulations of priming within the left temporal lobe (red) showed repetition suppression for congruent pairs and repetition enhancement for incongruent pairs at 20-39ms. The modulations of priming within the left frontal lobe (pink) showed repetition suppression for congruent pairs and repetition enhancement for incongruent pairs at 143-162ms.

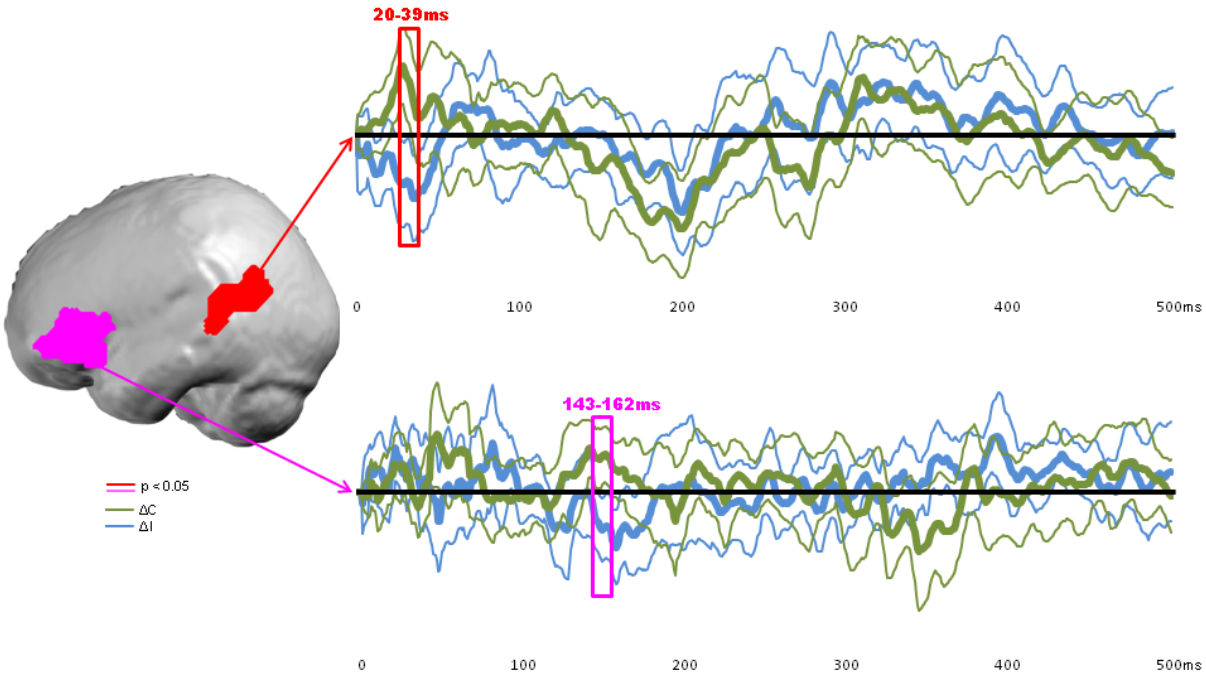


**Figure 14. Statistical analyses different from zero.**

The left temporal region in red (corresponding to the cluster of significant difference between conditions ΔC and ΔI) showed a mean activity that is also different from zero over the same time period (as well as later, around 200ms post-stimulus onset; upper graph). The left frontal region in pink (corresponding to the cluster of significant difference between conditions ΔC and ΔI) showed a mean activity that is also different from zero over the same time period (bottom graph). The activity of the cluster under the conditions ΔC and ΔI are represented in blue and green, respectively (mean in bold line, confidence interval in thin lines).

Over the 143-162ms post-stimulus onset period, a left frontal cluster comprising the inferior and partially the middle frontal gyri yielded repetition suppression for congruent and repetition enhancement for incongruent pairs. Posthoc analysis revealed that during this time window the repetition suppression in congruent pairs and the repetition enhancement in incongruent pairs were statistically significant. Indeed, the mean activity of the cluster was statistically different from zero over the 144-167ms and over the 144-160ms post-stimulus onset period for the congruent vs. incongruent condition, respectively (see Fig.14).

### *3.2.3.b Lateralization independent priming effects*

Temporo-spatial patterns of neural activity associated with position-independent representations were identified by comparing initial presentations vs. repeats, independently of congruency. The time frame-wise paired t-tests with factor of presentation (IP vs. RP)

performed on source estimations were applied to all solution points. The analysis revealed three clusters of solution points exhibiting significant priming effect (Fig.15).

Over the 42-63ms post-stimulus onset period, three individual clusters within the right fronto -temporal region yielded statistically significant repetition enhancement. The individual clusters comprised i) the posterior part of the inferior frontal gyrus and anterior part of the insula; ii) the anterior parts of the middle and superior temporal gyri; and iii) the fusiform and parahippocampal gyri, the hippocampal formation and the amygdale.

Over the 165-215ms post-stimulus onset period, a large cluster within the left hemisphere yielded statistically significant repetition suppression. It comprised the posterior parts of the supratemporal plane (including Heschl's gyrus and planum temporal) and of the superior, middle and inferior temporal gyri; the fusiform, lingual and middle occipital gyri; the inferior parietal lobule and the inferior part of the superior parietal lobule.

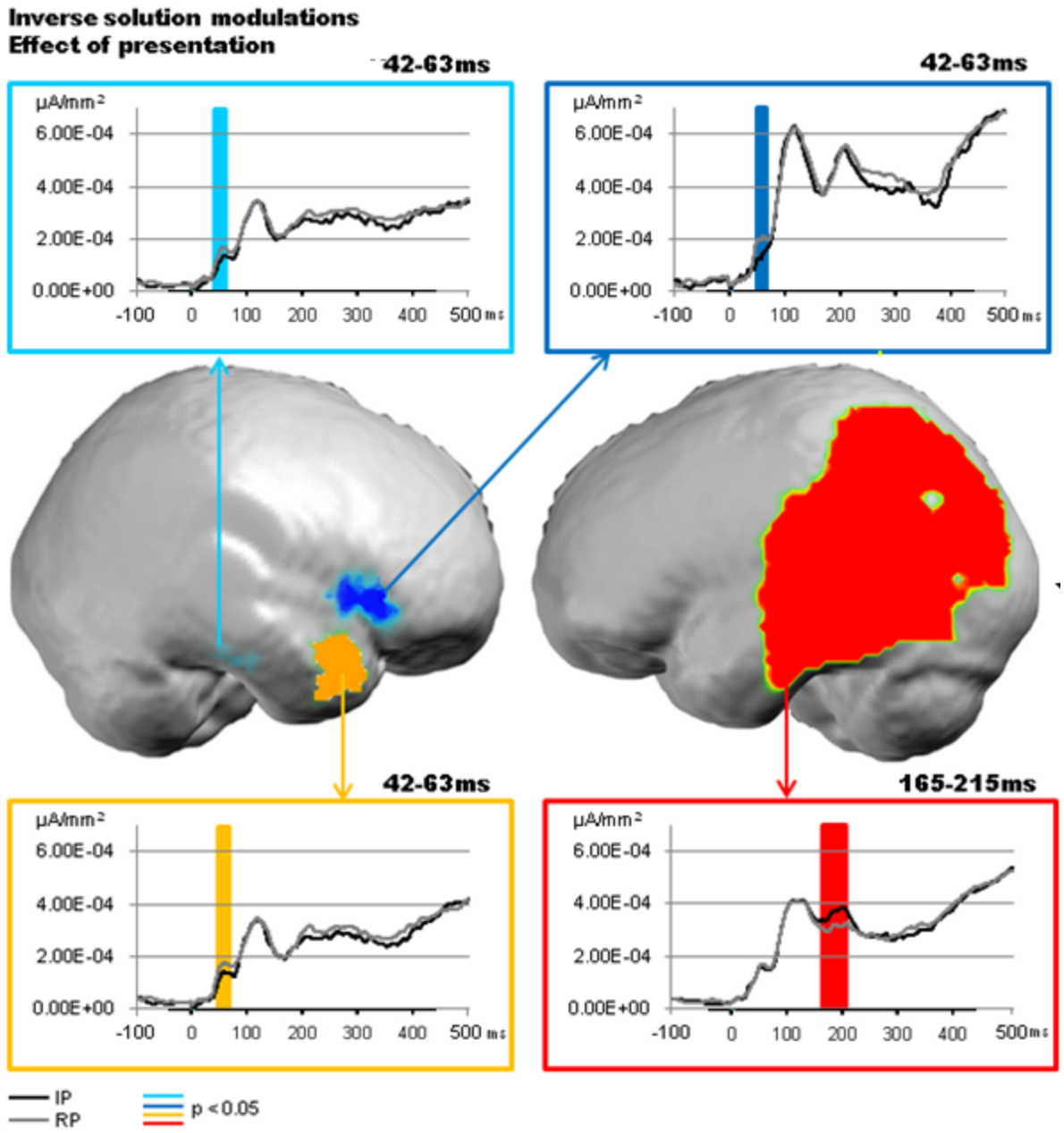


**Figure 15. Inverse solution modulations.**

Effect of presentation. Four clusters exhibited significant effect of presentation. The right middle temporal (the light blue cluster), right frontal (the dark blue cluster) and right anterior temporal (the orange cluster) brain regions showed repetition enhancement over the 42-63ms post-stimulus onset period. The left temporo-parietal brain region (the red cluster) exhibited significant repetition suppression over the 165-215ms post-stimulus onset period. The modulations of neural activity within the these clusters are represented in black for IP and grey for RP conditions, in the top left panel for the right middle temporal region (light blue), in the top right panel for the right frontal region (dark blue), in the bottom left panel for the right anterior temporal region (orange), and in the bottom left panel for the left temporo-parietal brain region (red).

Additional analyses were conducted on the same data set using a three ways ANOVA with factors of presentation (IP vs. RP), congruency (C vs. I) and side of the sound (L vs. R). Importantly, the factor of congruency is not orthogonal to the other factors; this is indeed a violation of the assumptions that allow the use of the ANOVA. Thus, the following analyses were solely exploratory and were not discussed further; however, they summarize important additional aspects of the data. One might notice an effect of side involving the left hemisphere over the 80-188ms post-stimulus onset period, as well as the right hemisphere over the 80-174ms post-stimulus onset period (Fig.16 and Fig.17, respectively), indeed, sounds elicited stronger brain activities within the contralateral hemisphere.

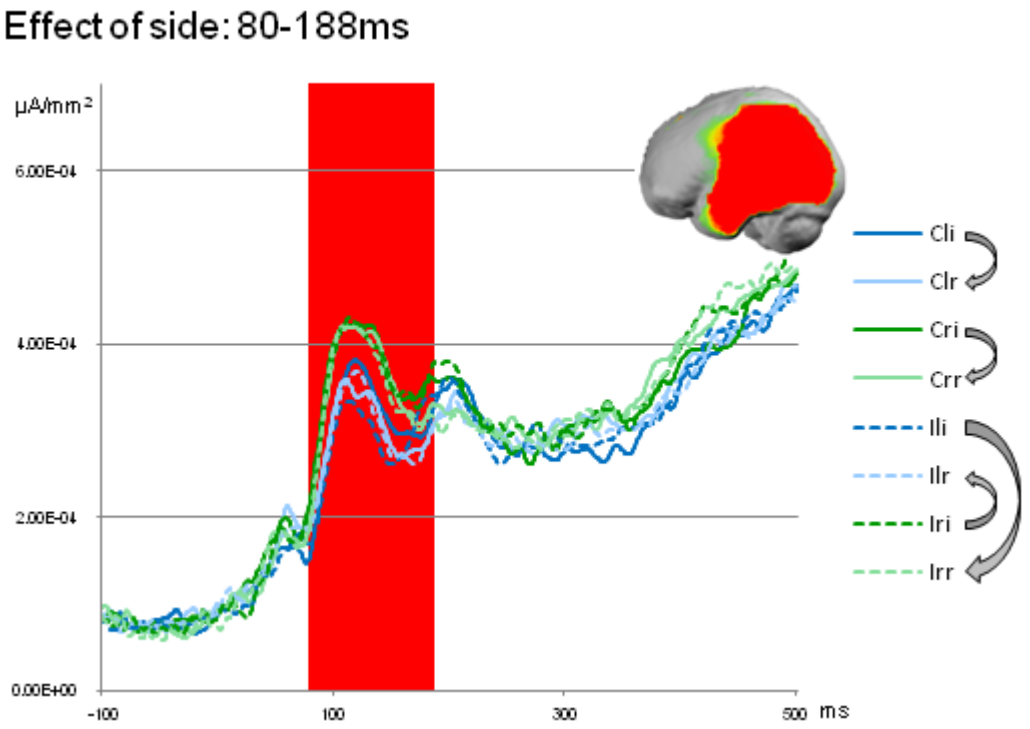


**Figure 16. Effect of side of the three ways ANOVA. Left hemisphere.**

A cluster on the left hemisphere (red portion on the brain) showed an effect of factor side over the 80-188ms post-stimulus onset period (in red). C: sounds from congruent pairs, I: sounds from incongruent pairs, li: sounds from the left side and presented as initial, lr: sounds from the left side and presented as repeated, ri: sounds from the right side and presented as initial, rr: sounds from the right side and presented as repeated. The arrows represent the sound pairs: within congruent pairs the initial and the repeated sounds were presented at the same side, whereas it's the opposite within the incongruent pairs. Note that during the 80-188ms post-stimulus onset period the green curves are higher than the blue curves representing the sound presented to the right vs. left side, respectively.

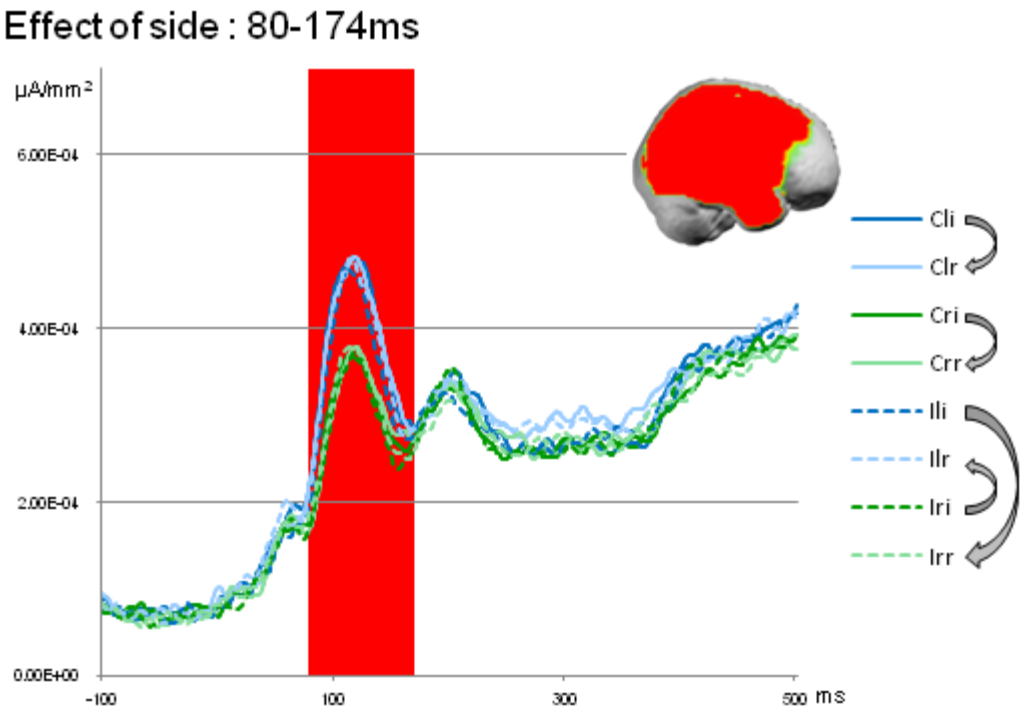


**Figure 17. Effect of side of the three ways ANOVA. Right hemisphere.**

A cluster on the right hemisphere (red portion on the brain) showed an effect of factor side over the 80-174ms post-stimulus onset period (in red). C: sounds from congruent pairs, I: sounds from incongruent pairs, li: sounds from the left side and presented as initial, lr: sounds from the left side and presented as repeated, ri: sounds from the right side and presented as initial, rr: sounds from the right side and presented as repeated. The arrows represent the sound pairs: within congruent pairs the initial and the repeated sounds were presented at the same side, whereas it's the opposite within the incongruent pairs. Note that during the 80-174ms post-stimulus onset period the blue curves are higher than the green curves representing the sound presented to the left vs. right side, respectively.

Regarding the main effect of presentation, the three ways ANOVA revealed two relevant clusters (Fig.18 and Fig.19). The first cluster involved the right middle temporal, frontal and anterior temporal brain regions over the 40-63ms post-stimulus onset period, like I reported above in the two ways ANOVA (see Fig.15 and Fig.18). While the second cluster involved the left temporo-parietal brain region over the 163-220ms post-stimulus onset period, like I reported above in the two ways ANOVA (see Fig.15 and Fig.19). Interestingly, neither interaction of the factors side and presentation nor the interaction of the factors of side and congruency was found at these latencies.

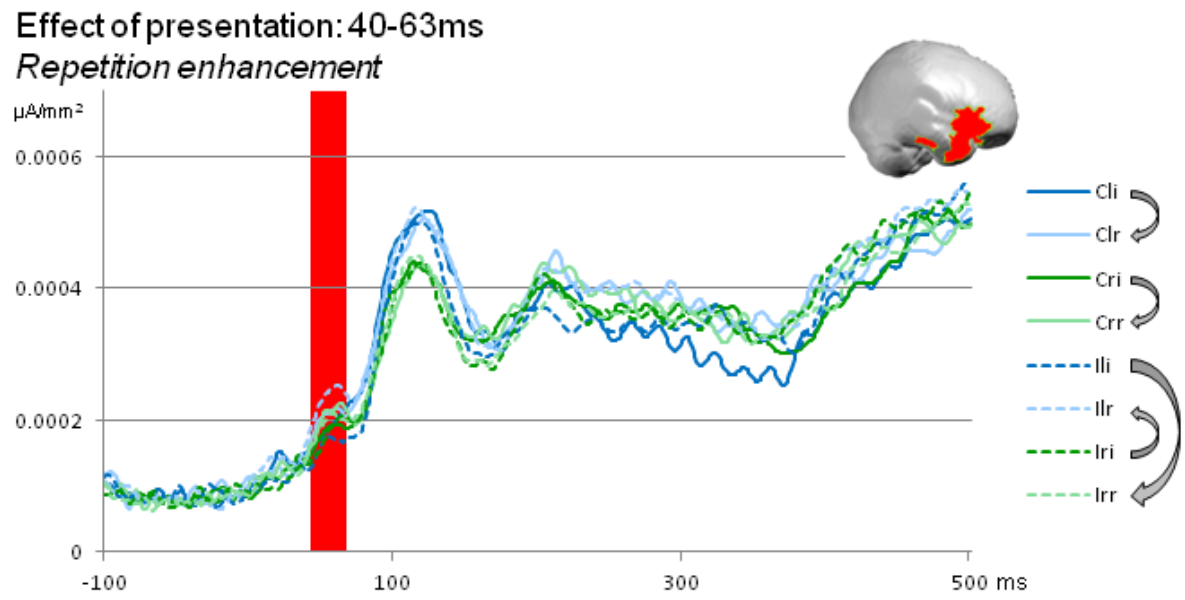


**Figure 18. Effect of presentation of the three ways ANOVA. Repetition enhancement.**

A cluster on the right hemisphere (red portion on the brain) showed an effect of factor presentation over the 40-63ms post-stimulus onset period (in red). C: sounds from congruent pairs, I: sounds from incongruent pairs, li: sounds from the left side and presented as initial, lr: sounds from the left side and presented as repeated, ri: sounds from the right side and presented as initial, rr: sounds from the right side and presented as repeated. The arrows represent the sound pairs: within congruent pairs the initial and the repeated sounds were presented at the same side, whereas it's the opposite within the incongruent pairs. Note that during the 40-63ms post-stimulus onset period the light curves are higher than the dark curves representing the repeated vs. initial presentation of the sound, respectively.

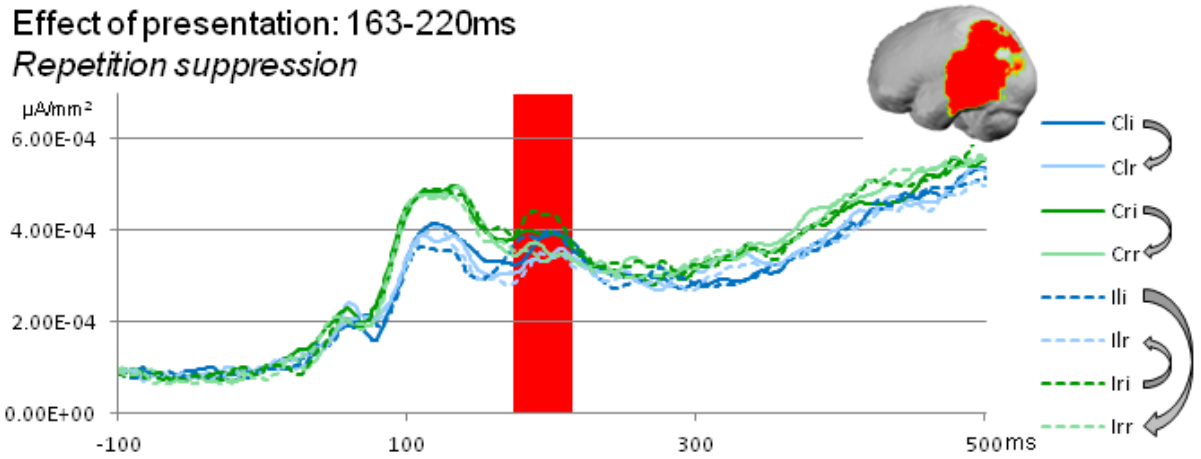


**Figure 19. Effect of presentation of the three ways ANOVA. Repetition suppression.**

A cluster on the left hemisphere (red portion on the brain) showed an effect of factor presentation over the 163-220ms post-stimulus onset period (in red). C: sounds from congruent pairs, I: sounds from incongruent pairs, li: sounds from the left side and presented as initial, lr: sounds from the left side and presented as

repeated, ri: sounds from the right side and presented as initial, rr: sounds from the right side and presented as repeated. The arrows represent the sound pairs: within congruent pairs the initial and the repeated sounds were presented at the same side, whereas it's the opposite within the incongruent pairs. Note that during the 80-174ms post-stimulus onset period the dark curves are higher than the light curves representing the initial vs. repeated presentation of the sound, respectively.

## 3.3 Plasticity of the motor representations of action sounds (study C)

The aim of this study was to investigate the plasticity of the motor representations of action sounds. More specifically, I hypothesized that the motor representations of action sounds share the priming-induced plasticity with the semantic representations within the ventral/What stream. MEPs induced by TMS single pulses were recorded from a hand muscle (i.e. the FDI) of both hands. An example of individual MEPs recorded from the left hand of a volunteer under right motor cortex stimulation is presented in Fig.20.

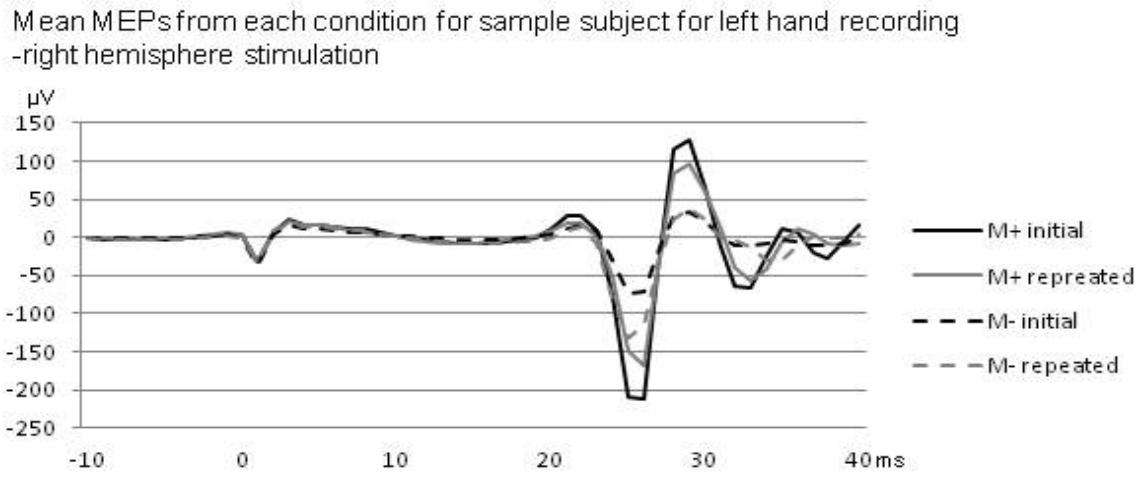


**Figure 20. Typical MEPs from the left hand of a sample subject.**

The MEPs were recorded from the left hand upon right motor cortex stimulation. Black lines represent the MEP obtained for initial presentations and grey lines represent the MEP obtained for repeated presentations. Plain lines represent the MEP obtained with sounds of category M+ and dotted lines represent the MEP obtained with sounds of category M-.

### 3.3.1 MEPs from the left hand upon right hemisphere TMS

A repeated measure ANOVA revealed a significant effect of category ($F_{(1,14)}$=5.12; p<0.05), a marginally significant effect of presentation ($F_{(1,14)}$=3.72; p=0.07) and a significant interaction of the factors category and presentation ($F_{(1,14)}$=8.12; p<0.05). Post-hoc t-tests revealed that the repeated presentation of M+ sounds yielded significantly smaller MEPs than initial presentations ($T_{(1,14)}$=2.66; p<0.05; Fig.21); no statistically significant difference was observed between MEPs associated with the initial and repeated presentations of M- sounds ($T_{(1,14)}$=0.95; p=0.36). The MEPs associated with the initial presentation were significantly larger for M+ than M- sounds ($T_{(1,14)}$=2.88; p<0.05); no significant difference was observed between MEPs associated with the repeated presentation of M+ and M- sounds ($T_{(1,14)}$=0.66; p=0.52).

### 3.3.2 MEPs from the right hand upon left hemisphere TMS

A repeated measure ANOVA revealed a marginally main effect of category ($F_{(1,15)}$=3.98; p=0.06); the main effect of presentation and the interaction effect between the factors were not significant ($F_{(1,15)}$=1.20; p=0.29; $F_{(1,15)}$=0.02; p=0.90, respectively). The trend I observed was that MEP amplitudes were greater when the TMS pulse was associated with a M+ than a M- sound (Fig.21).

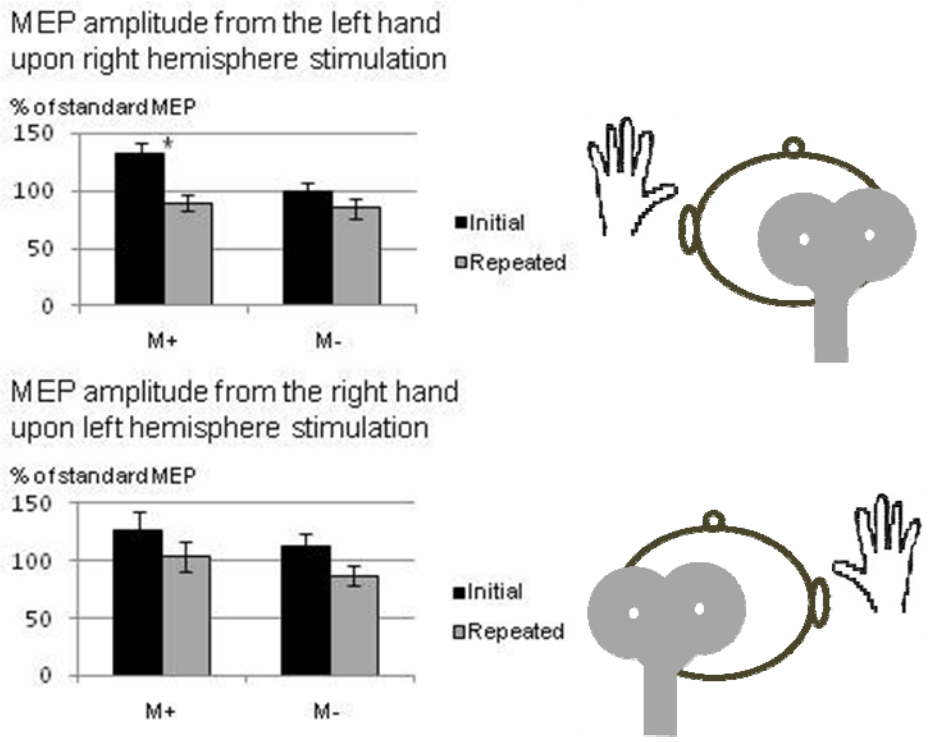


**Figure 21. MEP response modulations normalized by standard MEP.**

The amplitude of the MEPs of the left hand upon right motor cortex TMS (upper panel) showed significantly greater amplitudes of the MEPs when the TMS pulse was associated with a sound of category M+ compared to a category M-. The interaction effect of the factors (category by presentation) was also significant. Post-hoc t-tests revealed a significant effect of presentation for the M+ sounds, but not for the M- sounds. The amplitude of the MEPs of the right hand upon left motor cortex TMS (bottom panel) showed no significant effect. Black bars represent the amplitude of the MEPs obtained for initial presentations and grey bars represent the amplitude of the MEPs obtained repeated presentations.

# CHAPTER 4 DISCUSSION

## 4.1 Impact of the temporal history of exposure to sound objects on their cortical representations (study A)

The aim of this study was to investigate the impact of the temporal history of exposure to sound objects on their cortical representations. More specifically, I hypothesized that a recent, single exposure to a sound object and a repeated, frequent exposure to it modulate in a different way the temporal-spatial patterns of neural activity that underlie sound recognition.

I found a cluster of solution points within the left temporal convexity exhibiting repetition suppression for the main effect of presentation as well as two cluster of solution points showing repetition suppression effect for the main effect of section, one located within the left temporal convexity and the second cluster within the right temporoparietal junction (see Fig.11 and Fig.22).

My results speak in favor of differential sound object representations within the auditory cortex, as a function of the temporal history of exposure to these objects. Often heard sounds are coded by a modulation in a bilateral network. Recently heard sounds, independently of the number of previous exposures, are coded by a modulation of a left-sided network (see Fig.22).

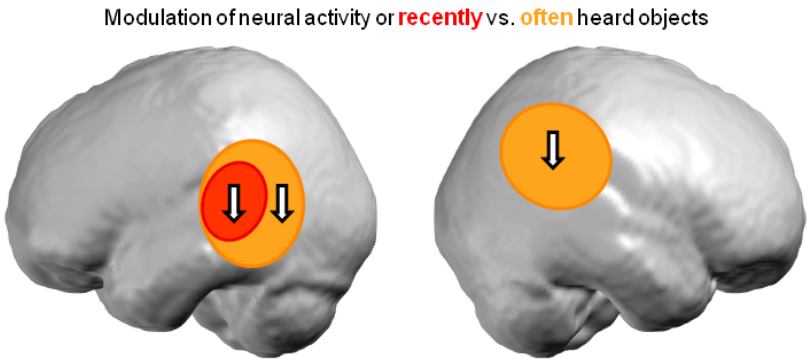


**Figure 22. Modulation of neural activity for recently vs. often heard object.**

The region in red showed plastic representations for recently heard objects, the regions in orange showed plastic representations for often heard objects both at ca 150-220ms post-stimulus onset. The down arrows represent repetition suppression.

### 4.1.1 Neural plasticity related to multiple presentations of a sound object

Repetition suppression for often heard sounds, here after 24 to 31 presentations stretching over 72 to 132min. (factor section), was present approximately at the same post-stimulus time period in both hemispheres. On the left side it involved the planum temporale; the posterior parts of the superior, middle and inferior temporal gyri; and the supramarginal and angular gyri at 152-199ms, and on the right side the planum temporale; the posterior parts of the superior and middle temporal gyri; and the superior and inferior parietal lobules at 162-221ms post-stimulus onset.

Importantly, I report here the effect of multiple exposures to a sound object occurring over a long period of time (factor of section). However, the present study cannot disentangle the specific effect of the number of stimulus exposures from the specific effect of the duration of the sections of the experiment.

The regions that displayed a significant suppression through multiple presentations correspond on the left side to the posterior part of the auditory ventral/What stream and on the right side to the intersection between the dorsal/Where and the ventral/What streams (Alain et al., 2001; Anourova et al., 2001; Arnott et al., 2004; De Santis et al., 2007; Maeder et al., 2001).

They include areas for which suppression was described following (few) repetitions in paradigms ranging from feature analysis to categorization of environmental sounds:

- bilateral superior temporal gyrus posterior to Heschl's gyrus, which was shown to decrease the BOLD signal during repeats of spectral and amplitude envelopes of animal vocalizations (Altmann et al., 2010).

- bilateral superior temporal sulcus and the right superior temporal gyrus, which displayed a decrease in BOLD signal associated with repetition of blocks of (acoustically identical) environmental sounds (Bergerbest et al., 2004).

- bilateral superior temporal gyrus, which yielded suppression to the repetition of acoustically -identical or -different exemplars of sound objects (De Lucia et al., 2010b).

- left superior temporal and posterior middle temporal gyri, which displayed category specific repetition suppression, to animal vocalizations and tool sounds, respectively (Doehrmann et al., 2008).

The time window of the repetition suppression due to multiple presentations is comparable to that described with few repetitions; using the same sound tracks (but not lateralized) in another study (Murray et al., 2008a). Repetition suppression has been observed over 156-215ms within the left middle temporal gyrus and superior temporal sulcus. In magnetoencephalographic recordings adaptation effects were reported for the P2m component, which occurred at ca. 200ms post-stimulus onset (Altmann et al., 2008).

The involvement of the right inferior parietal cortex may be due to the spatial attributes of the stimuli, which were absent in previous repetition priming paradigms. Such an interpretation is in agreement with a recent study which used spatially localized animal vocalizations in repetitive presentations with intermittent changes in animal identity or location. For location

changes, as compared to rest, significant increases of BOLD responses were found bilaterally in planum temporale and posterior superior temporal gyrus; for location versus animal changes, significant increases occurred in the right temporo-parietal junction and the anterior insula as well as bilaterally in the inferior parietal lobule (Altmann et al., 2007).

Thus, plastic changes which occur after multiple presentations of lateralized sound objects involve relatively large networks, encompassing perceptual and semantic stages of the auditory ventral/What stream as well as parts of the dorsal/Where stream.

### 4.1.2 Neural plasticity related to recently heard objects

Recent repetition of lateralized environmental sounds, here within 2-12sec. after the prime (factor presentation), yielded suppression at 182-215ms post-stimulus onset in the left planum temporale and posterior parts of the left superior and middle temporal gyri. The suppression effect was limited to regions of the temporal convexity that were shown to carry the semantic representations within the auditory ventral/What stream (Scott, 2005; Leaver and Rauschecker, 2010). It occurred within a similar location and time window as in previous studies using sounds of the same (Doehrmann et al., 2008; Murray et al., 2008a) or acoustically different exemplars of non-lateralized environmental sounds (De Lucia et al., 2010b).

Together, these studies suggest that keeping track of recently heard objects taps into the plasticity of associative-semantic (rather than perceptual-discriminative) representations, where positional information may not have a strong influence on coding. The occurrence of position-independent repetition priming effects within the auditory ventral/What stream is reminiscent of a similar organization within the visual cortex. Repetition suppression within extrastriate occipital areas occurred independently of whether repeated stimuli differed in size, position, illumination or viewpoint (Grill-Spector et al., 1999; Vuilleumier et al., 2002). Further along the visual What and Where pathways the viewpoint had, however, differential influence on repetition effects. Within the ventral temporo-occipital cortex (the visual What pathway) repetition suppression was the same for stimuli that were rotated or not with respect to the prime while within the posterior intraparietal sulcus (i. e., the visual Where pathway)

repetition suppression was present only for the same target orientation, while rotated targets were perceived as new (James et al., 2002).

Thus, plastic changes that occur after recent exposure to the same sound object appear to be limited to parts of its semantic representation within the left auditory ventral/What stream. Unlike plastic changes associated with multiple repetitions, they concentrate on the "common denominator" of the stimuli (here the semantic representation) and do not encompass the perceptual or spatial features of the stimuli, which tended to vary between primes and repeats.

### 4.1.3 Spatio-temporal brain dynamics for keeping track of temporal history of exposure

The existence of different networks that keep track of different stimulus characteristics, albeit not temporal history, has been demonstrated by priming experiments in visual cortex. Within the fusiform face area famous faces yielded greater repetition suppression than unfamiliar faces (Henson et al., 2000) and heavily degraded (Dolan et al., 1997) or difficult to recognize face images (George et al., 1999) were accompanied with repetition enhancement. On the parieto-temporo-occipital cortex different patterns of repetition effects were observed for familiar vs. globally non-familiar drawings (Soldan et al., 2008b) or for drawings of possible vs. impossible non-existing objects (Soldan et al., 2008a).

To my knowledge this is the first demonstration of the spatio-temporal brain dynamics which keep track of the temporal history of exposure to sound objects. My results indicate that rapidly occurring plastic changes within the left hemisphere keep track of sounds heard a few seconds before, independently of a more general sound exposure history. Progressively occurring and more long-lasting plastic changes within both hemispheres keep track of the history of the sound exposure over a larger time scale including numerous repetitions. The presence of short-term changes associated with recent exposure independently of a history of multiple repetitions, suggests that different neural populations and/or mechanisms sustain neural plasticity related to recently vs. often heard objects. The involvement of different neural populations is partially demonstrated by the different spatial distributions of the main effects of presentation and section. The neural mechanisms remain, however, unclear, since

either type of plasticity could be sustained by the sharpening of neural representations or a general decrease in firing rate (Grill-Spector et al., 2006).

## 4.2 Coding of sound objects which carry spatial information (study B)

The aim of this study was to investigate the impact coding of sound object carrying spatial information. More specifically, I hypothesized that a sound object which carries positional information activates, at the cortical level, both a position-independent and a position-linked representation. I explored these representations with a repetition priming paradigm.

The analyses of position-independent representations revealed repetition enhancement within three clusters of solution points located at the right fronto-temporal region over the 42-63ms post sound onset period, as well as repetition suppression within a large temporo-parietal region over the 165-215ms post sound onset period (see Fig.15 and Fig.23).

The analyses of position-linked representations showed repetition suppression for spatially congruent sound pairs over the 20-39ms post sound onset period within the left temporal region and over the 143-162ms post sound onset period within the frontal brain region. In the contrary, repetition enhancement were observed for spatially incongruent sound pairs over the same time periods and within the corresponding brain regions (i.e. over the 20-39ms post sound onset period within the left temporal region and over the 143-162ms post sound onset period within the frontal brain region) (see Fig 13, Fig.14 and Fig.23).

My results reveal an ultrarapid discrimination of sound objects which are characterized by spatial cues and suggest that this discrimination involves two temporo-spatially distinct cortical representations (see Fig.23), as well as position-independent representations of sound objects.

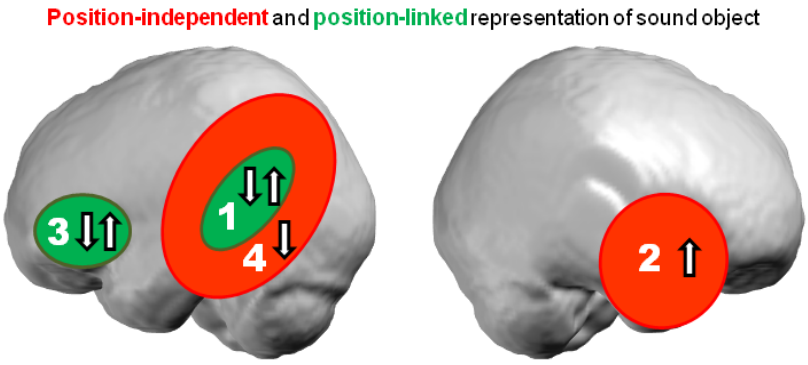


**Figure 23. Position-independent and position-linked representation of sound object.**

The regions in red are involved in position-independent representation of sound object. The regions in green are involved in position-linked representation of sound objects. The numbers represent temporal sequence of the involvement of the different networks during sound processing. The down arrows represent repetition suppression, the up arrows represent repetition enhancement. In position-linked representations repetitions in identical positions lead to repetition suppression, in different positions to repetition enhancement.

### 4.2.1 Ultra rapid discrimination

Using sound objects with spatial characteristics revealed very early repetition effects as 20-39ms and 42-63ms post stimulus onset periods. This is well before later effects at 143-162 and 165-215ms, which occurred at roughly the same time window as in previous studies with non-lateralized environmental sounds (Altmann et al. 2008; Murray et al. 2008a).

Very short latencies for stimuli with spatial cues have been reported previously in magnetoencephalographic studies. In a task of passive listening to tone bursts lateralized with interaural time differences first modulations of neural activity by position occurred at N20m in the superior temporal gyrus and the middle frontal region on the right side and at N50m in prefrontal and parietal regions (Itoh et al. 2000). Short clicks delivered to the left ear yielded peak latencies at 28ms in medial and at 33ms in lateral Heschl's gyrus; at 38ms in posterior parietal cortex; at 35-50ms in the posterior part of the superior temporal gyrus; at 48ms in the anterior part of the superior temporal gyrus; and at 76ms in the planum temporale (Inui et al. 2008). The sound of a knife tapping on a glass delivered at different azimuthal positions yielded neuronal activity which was modulated by spatial position at 40-60ms bilaterally in medial and at 100ms in lateral Heschl's gyrus; and at 180 in the right posterior superior temporal gyrus (Brunetti et al. 2008). Categorization of living vs. man-made sound sources

has been reported as early as 70ms (Murray et al., 2006; see De Lucia et al., 2010a and Fig.3 of the introduction chapter for a general timing of sound object processing).

### 4.2.2 Position-independent sound object representations

Independently of lateralization cues repeated exposure to sound objects yielded significant repetition effects during two time periods, suggesting the existence of a temporo-spatial pattern of neural activity which underlies position-independent sound object representations.

The most prominent effect was a repetition suppression which occurred on the left hemispheric convexity at 165-215ms post-onset period. Its independence from lateralization cues - it was significant for both congruent and incongruent pairs – strongly suggests that it reflects solely the semantic identity of primes and repeats. The existence of a semantic sound object representation that is independent of positional information is a major confirmation of the dual-stream model of auditory semantic vs. spatial processing (Romanski et al., 1999; Kaas and Hackett, 1999; 2000; Rauschecker and Tian, 2000; Tian et al., 2001; Maeder et al., 2001; Alain et al., 2004; Arnott et al., 2004; Scott, 2005; Rauscheker and Tian, 2000; Rauschecker and Scott, 2009; Leaver and Rauschecker, 2010; van der Zwaag et al., 2011). It is interesting to note that the repetition suppression presented here occurred over a time period that is very similar to that described in previous studies which used not-latereralized environmental sounds (Altmann et al. 2008; Murray et al. 2008a), but that the priming effect involved here larger parts of the left convexity. In particular I observed not only the involvement of the ventral/What stream as in previous EEG and fMRI studies (Bergerbest et al., 2004; Altmann et al., 2008; Murray et al., 2008a; De Lucia et al., 2010b), but also a contribution of the dorsal/Where stream.

A very early, but shorter and less extensive effect was a repetition enhancement which occurred in the anterior and inferior temporal and ventral prefrontal cortices on the left side at 42-63ms post-onset. The enhancement occurred independently from lateralization cues, both for congruent and incongruent pairs; reflecting thus solely the semantic identity between primes and repeats. No priming effect was reported at this time window in previous studies, which used non-lateralized environmental sounds (Altmann et al., 2008; Murray et al.,

2008a). Hence it may reflect activity in a neural population which codes for semantic and spatial aspects of sound objects, but is selectively modulated by semantic content. Such an interpretation is supported by electrophysiological studies in non-human primates. Neurons within the ventral prefrontal region were found to be modulated by both the location and the type of the auditory stimulus (Cohen et al. 2004) although their response characteristics during specific tasks suggested that they are primarily part of the non-spatial, ventral auditory pathway (Cohen et al. 2009).

### **4.2.3** Position-linked representations of sound objects

Different priming effects in congruently vs. incongruently lateralized patterns was found during two time periods, when repetition suppression occurred during the repeat of the same object at the same lateralization and repetition enhancement for the same object at different lateralization. This observation speaks in favor of position-linked sound object representations.

A very early priming effect occurred on the posterior part of the left superior temporal gyrus at 20-39ms post stimulus onset. In a previous MEG adaptation study this same region was shown to respond more strongly to probes preceded by spatially than by phonetically different adaptors and hence more likely to be more sharply tuned to spatial than phonetic information (this effect occurred, however, later, at 70-150ms (Ahveninen et al. 2006).

The second priming effect occurred on the left inferior frontal gyrus at 143-162ms post stimulus onset, in a region which is likely to be part of the ventral/What pathway. In non-human primates the ventral/What stream is believed to include the ventral prefrontal cortex, which is strongly interconnected with the (auditory) antero-lateral belt areas (Romanski and Averbeck, 2009), but where neurons were found to be modulated by both the location and the type of an auditory stimulus (Cohen et al. 2004).

Lemus et al., (2009) reported neural activity related to auditory working memory task involving the What processing (fluttering rate discrimination) within the ventral premotor cortex of monkeys.

### 4.2.4 Dual representation for sound objects

My results strongly support a dual representation of sound objects, with a position-independent and a position-linked coding. The neural networks underlying either representation involve predominantly the ventral/What pathway.

In natural settings a sound object is characterized by its identity and its location. Importantly, while the identity is stable over time, the location of the sound source may vary. Thus, the ability to create valuable representation of the environment we need to match the identity of the sound source with its various locations over time. I believe that the position-linked representations of the sound object play an important role for this matching processing.

In the visual domain, repetition priming paradigms revealed a similar dichotomy in spatially-independent and –dependent representations. Within extrastriate occipital areas repetition suppression occurred independently of whether repeated stimuli differed in size, position, illumination or viewpoint (Grill-Spector et al. 1999). Further along the visual What and Where pathways the viewpoint had, however, differential influence on repetition effects. Within the ventral temporo-occipital cortex (the visual What pathway) response suppression was the same for repeated stimuli that were rotated or not in respect to the prime while within the posterior intraparietal sulcus (i. e., the visual Where pathway) response suppression was present only for the same target orientation, while rotated targets were perceived as new (James et al. 2002). Furthermore, hemispheric differences were observed within the ventral pathway, with view-independent priming in the left fusiform and a view-dependent priming in the right fusiform gyrus (Vuilleumier et al. 2002). The existence of representations of visual objects that are invariant over the relative size and locations of the stimuli is further supported by electrophysiological recordings from macaque inferotemporal cortex (Lueschow et al., 1994; Booth et Rolls, 1998).

### 4.2.5 Repetition enhancement

The observation of repetition suppression and repetition enhancement is influenced by several parameters such as the familiarity of the stimulus, the possibility to name the object, the quality (degraded or not) of the stimulus, its duration as well as contribution from the episodic

memory (Gauthier, 2000). Three different mechanisms may underlie the repetition enhancement observed in this study.

First, repetition enhancement is likely to reflect changes in one of the object characteristics which were monitored by the network. In my study this was the case for repetition enhancement observed for incongruent pairs (as opposed to the repetition suppression for congruent pairs) at 20-39 and 143-162ms post stimulus. Repetition enhancement in response to specific features of the stimulus has been reported previously for frequency-modulated tones; repetition enhancement characterized pairs of up-up sweeps, but not of up-down sweeps or of unmodulated tones; the authors hypothesized that the enhancement effect was yielded by a network monitoring consecutive sounds and thus sensitive to the frequency separation between the end of the initial and the beginning of the repeated sweep (Heinemann et al. 2010).

Second, repetition enhancement could reflect the first stages of the formation of a memory trace, as described in previous fMRI studies of visual or auditory-verbal priming (Blondin and Lepage, 2005; Buchsbaum and D'Esposito, 2009). This interpretation could be relevant for repetition enhancement which occurred at 42-63ms post stimulus onset in regions including the parahippocampal gyrus and hippocampal formation. It concerned the position-independent representation and characterized both repeats with the same or with different lateralization. The hippocampal involvement suggests that spatial cues may convey an episodic feature to a sound object.

Finally, repetition enhancement could reflect the degree of difficulty of the comparison, as demonstrated for repetition priming with impossible or unfamiliar visual objects (Soldan et al., 2008a; 200b), or face images that were unfamiliar or difficult to recognized (George et al., 1999; Henson et al., 2000). In monkeys familiar stimuli elicit less activity from neurons of the prefrontal cortex region than unfamiliar stimuli (Rainer and Miller, 2000). In my material it may reflect the degree of difficulty to compare sound objects on the basis of the first few milliseconds.

## 4.3 Plasticity of the motor representations of action sounds (study C)

The aim of this study was to investigate the plasticity of the motor representations of action sounds. More specifically, I hypothesized that the motor representations of action sounds share the priming-induced plasticity with the semantic representations within the ventral/What stream.

The results obtained when stimulating the left hemisphere and recording the right hand muscle were in accordance with those of Aziz-Zadeh et al., (2004), as I obtained a marginally significant effect of sound category (M+ associated with stronger motor responses than M- sounds). Regarding the stimulation of the right hemisphere and the recording the left hand muscle, I obtained a significant effect of category, which was not found by Aziz-Zadeh et al., 2004). More interestingly, I reported an interaction effect between the factor of presentation and the factor of category. I observed repetition suppression of the motor response within the M+ but not within the M- category (see Fig.21).

My results suggest a specific involvement of the right hemisphere for the processing of action related sounds. Indeed, the cortical representations of action within the right hemisphere underwent repetition-induced plasticity, as reveled by repetition suppression measurements.

### 4.3.1 Repetition suppression in motor representations of action sounds

Repetition priming of motoneuronal activity has been previously described in the feeding network of aplysia, where repeated stimulation lead to an increase in the firing rate of neurons (Friedman et al., 2009). The repetition enhancement has been interpreted as an intrinsic characteristic of a network dedicated to motor behavior (Friedman and Weiss, 2010). To my knowledge my work is a first demonstration of repetition suppression in motor output, which suggests that motor representations of action sounds share at least some of the neural mechanisms of auditory semantic representations.

Neural networks which sustain repetition suppression in perceptual and semantic representations of environmental sounds (Bergerbest et al., 2004; Doehrmann et al., 2008; Altmann et al., 2008; Murray et al., 2008a; De Lucia et al., 2010b) share this characteristic with action-sound representations in (left) premotor cortex (Pizzamiglio et al., 2005). The action-sound representation within the premotor and motor cortices (Hauk et al., 2006) is believed to provide input to motor neurons, which increases the excitability of motor neurons during the presentations of action sounds; increased excitability has been demonstrated in TMS paradigms (Aziz-Zadeh et al., 2004). The repetition-induced MEP suppression which I observed for action sounds is likely to be due to a repetition suppression of afferents from action representations of sounds upon motor neurons.

In my study MEPs associated with MA+ sounds were on average larger than those associated with MA- sounds. The difference was statistically significant for left TMS and right MEPs and marginally significant for right TMS and left MEPs. As the alpha criterion of 0.05 is only a consensual convention, the marginally effect (p-value = 0.06) obtained for the category effect when stimulating the left hemisphere is not in contradiction with the results of Aziz-Zadeh et al., (2004). However, the results obtained when stimulating the right hemisphere speaks in favor of a putatively different lateralization than reported by Aziz-Zadeh et al., (2004), in which significant increase of excitability was shown for left TMS and right MEPs, but not for right TMS and left MEPs. Aziz-Zadeh and colleagues used only two hand-related sounds, typing and tearing paper, with 20 repetitions of each. My results, based on a variety of 30 action sounds, have demonstrated clearly a strong right hemispheric repetition suppression within the motor representation of action sounds. It is noteworthy that during the repeats MEP amplitudes were similar for action-related and –nonrelated sounds and this lack of difference due to repetitions could have driven the negative results concerning the right hemisphere in Aziz-Zadeh et al., (2004). Indeed, repeating sounds yields modulations of the brain response (Bergerbest et al., 2004; Murray et al., 2008a; Altmann et al., 2010; De Lucia et al., 2010b) that are sensitive to increasing number of sound presentations (Bourquin et al., a in preparation; study A). These modulations are believed to occur within neurons that are specifically involved in the stimulus processing such as motor and premotor cortex in action-related stimuli. Thus, using multiple times the same sound may have yielded to the comparison of differentially adapted brain activities.

In my study the priming effect within the M+ category was significant in the right but not in the left hemisphere. This asymmetry may be due to the fact that all the subjects were right-handed (suggestive of great lateralization of functions within the brain) and suggests a hemispheric difference in motor representations of action sounds. Several lines of evidence support this interpretation (Lewis et al., 2005; Gazzola et al., 2006; Lahav et al. 2007). Having learned to play a musical piece was shown to be accompanied by an increased activation within frontal regions, including Broca's area and the premotor cortex, during subsequent passive listening to the same melody (Lahav et al. 2007); the authors coined the term "hearing-doing" for this relationship. Within the left hemisphere the effect was important only for the learned melody, indicating a strong motor connection linked to the execution, whereas within the right hemisphere activation was generalized also to the learned notes in different melodies, suggesting a perceptual bias.

Regarding the modulations of brain responses obtained with motor learning, it is useful to consider the acquisition dynamics. Smyth et al., (2010) reported different patterns of cortical excitability depending on the dynamics of a motor acquisition (a wrist movement). Notably, they observed a decrease of the corticospinal excitability during the learning stage, followed by an increase of excitability once the motor acquisition had already been done 24 hours later. This study suggests that different brain patterns of cortical excitability can be observed depending on the skill of the person and the ongoing learning processes. Moreover, Lewis et al., (2005) reported both left and right hemisphere activity regions for right-handed participants when they were performing manipulation of virtual tools that had been previously presented visually. The authors interpreted the right hemispheric involvement as a manifestation of some form of visual or mental imagery of the motion dynamics associated with the action. In my study, we presented sounds of different expertise level to the volunteers: there were overlearnt sounds (e.g. clapping hands), sounds that arise from musical instruments that volunteers may have or not experience with (most of the volunteers had musical education for one up to five musical instruments), as well as environmental sounds that volunteers cannot have experience in producing them (e.g. storm).

### **4.3.2** Mirror neuron system

#### *4.3.2.a Mirror neurons described in non-human primates*

The mirror neurons were initially described in the macaque area F5, which is believed to represent the homologue of the Broca's area, for visually presented stimuli (Rizzolatti et al., 1996; Rizzolatti and Arbib, 1998; Rizzolatti et al., 2001). Mirror neurons responding to auditory stimuli have also been found in the macaque ventral premotor cortex (Kohler et al., 2002; Keysers et al., 2003; Romanski and Goldman-Rakic 2002; Kohler et al., (2002) where a neuronal population was active when the monkey performed or saw or heard a specific action. Moreover, these audiovisual mirror neurons were highly selective for a specific action and the patterns of activity were not significantly different regarding of the modality (motor vs. visual vs. auditory; Keysers et al., 2003). Thus, the prefrontal and premotor cortices underlie accurate action representations for perception of auditory stimuli. Interestingly, Romanski and Goldman-Rakic (2002) reported different patterns of responses to sounds within mirror neurons recorded in the prefrontal cortex. Some neurons were sensitive to the sound onset, some other were sensitive to the sound offset, while a large proportion (almost 50%) of the auditory mirror neurons exhibited sustained responses that lasted the length of the sound. The overwhelming majority of the auditory and visual mirror neurons was excitatory.

#### *4.3.2.b Mirror system in humans*

Mirror neurons have been also recorded in the human brain. Mukamel et al., (2010) studied visual mirror neurons in epileptic patients who had electrodes implanted prior to surgery. They found visual mirror neurons in the supplementary motor area, as well as in the hippocampus and the adjacent cortex. It is important to keep in mind that the recording sites of the electrodes were determined exclusively by clinical purposes and that the existence of mirror neurons in other parts of the human brain remains possible.

Evidence for mirror neurons in humans has been supported by observing brain regions that respond to both perceived and performed actions (e.g. Iacoboni et al., 1999; Gazzola et al., 2006; Lahav et al. 2007 Gazzola and Keysers, 2009). If the same neurons respond to both perceived and performed actions the brain region where they are located would have the same

property. However, the opposite is not true; observing a brain region that respond to both perceived and performed action does not mean that the activity is generated by the same neurons in both cases.

Mirror neurons in humans have been investigated through adaptation paradigms (e.g. Hamilton and Grafton, 2006; 2008). When a neural population is recruited for the processing of a second presentation of a stimulus, its activity is reduced. Thus, it is assumed that an adaptation effect observed for a particular type of stimuli when preceded by another type of stimuli is indicative of the existence of a neural population coding for both types of stimuli. In the auditory domain, neural suppression was observed within shared representations of conceptual (written words) and auditory actions (Pizzamiglio et al., 2005; Galati et al., 2008).

Rizzolatti and Sinigaglia, (2010) highlight the importance of the reproducibility of the action to activate the mirror system. The mirror system responds to actions produced by another species only if they are feasible by the observer. A human being does not bark and his mirror system does not respond to a dog barking, whereas it will be activated by a dog biting. The reproducibility of action involves a conceptual level that will allow various kinesthetic patterns. Aplastic patients (born without arms) showed activations in the classical regions of the mirror system when observing hand actions they cannot perform by hand but which they can reproduce the action goal with other effectors such as mouth or feet.

Several studies argued for a conceptual role of the mirror system in action representations. Costantini et al., (2008) reported repetition priming facilitation with images of actions performed with different effectors, they also reported facilitation for different targets. Galati et al., (2008) believe that the human mirror neuron system represents the meaning of action at an abstract level and is insensitive to the effector (hand or mouth) of the action (see also Rizzolatti & Sinigaglia, 2010). Moreover, Pizzamiglio et al., (2005) assessed the influence of actions represented at a conceptual level (written words) on the processing of environmental sounds related or not-related to actions. They found ERP modulations (repetition suppression) arising from the left posterior superior temporal region and the premotor area indicative of a conceptual coding for actions. Furthermore, Hamilton & Grafton, (2006; 2008) compared the

brain activity during the observation of action with the same vs. novel goal (defined by the target object). They reported repetition suppression within the left intraparietal sulcus and concluded that it encodes the goal of action. They also reported activation of the right parieto-frontal mirror circuit during intention understanding, suggestive of right hemispheric implication in intention understanding. The right inferior parietal lobe and right inferior frontal cortex showed repetition suppression when the same aim (outcome) is reached regardless of the kinematics of the movement. Thus, action representations by mirror neurons might not purely underlie perception or motor output but also reach a conceptual and abstract level of action representations.

### **4.3.3** The role of motor cortex in semantic representations

My results suggest that the motor representation of action sounds is part of semantic representations and not a remnant of a phylogenic or ontogenetic ready-for action system. Similar pieces of evidence of the implication of motor circuit for the stimulus processing have been shown for other sensory modalities such as vision (Fadiga et al., 1995; Aziz-Zadeh et al., 2002) and olfaction (Rossi et al., 2008). The involvement of primary motor cortex in the perception of action has been suggested by MEG (Nishitani & Hari, 2000) and ERP (Hauk et al., 2006) studies. It is currently, however, not clear how far this part of semantic representations is essential for successful recognition of action sounds. If motor representations of action sounds are essential, we predict that lesions of the motor cortex are associated with impaired recognition of action sounds. To our knowledge, this precise question has not been investigated, but two studies suggest a possible link between semantic and motor representations.

Pazzaglia et al., 2008 presented patients with left-hemisphere-damage causing limb and/or buccofacial apraxia and impairment of the recognition of action related to the hand and the face respectively, but not for non-action sounds. Thus, the recognition of hand and mouth action-related sounds was specifically impaired in patients with limb and bucco-facial apraxia, suggestive of a link between the motor and the perceptual systems. In addition, Chow et al., (2009) investigated the recognition of action sound in two populations of patients presenting neurodegenerative diseases (i.e. the corticobasal degeneration and the progressive supranuclear palsy) associated with cognitive and motor deficits. The recognition of action

sounds was impaired for these two patient populations compared to populations of patients with other degenerative diseases (the Alzheimer disease and the frontotemporal dementia). In addition, they showed that atrophy in the left pre-motor region selectively impairs the recognition of action sounds.

# CHAPTER 5 CONCLUSION

This work explored the representations of sound objects in time, space and action. There are multiple cortical representations of each sound object, encoding somewhat different stimulus features. Classically, the representations located within the ventral/What stream carry information about the identity of the sound sources, while the representations located within the dorsal/Where stream are sensitive to spatial information related to the sound source. Both types of sound representations are plastic, i.e. they can be modulated by the interactions with the environment.

I have demonstrated that the temporal history of the exposure to a sound object is highly relevant for the modulations occurring within the cortical representations of the sound objects. Indeed, differential sound object representations have been found within the auditory cortex for recently vs. often heard sounds. Multiple repetitions of the same sound object lead to a repetition suppression within a bilateral network, which is likely to keep track of a more general history of exposure to sound objects and might be relevant for long-term adaptation to the surrounding environment. Recently heard objects modulated -independently of the number of previous exposures- a left-sided network, suggesting that cortical representations keep track of experience over short-time latencies, regardless of a more general history of the exposure to the object. The independence of the two systems indicates that different neural populations and/or mechanisms sustain neural plasticity related to recently vs. often heard objects.

In addition, my work provides evidence for position-independent and position-linked representations of sound objects. The position-independent representation was characterized by repetition-induced plasticity which consisted of repetition enhancement within the right hemisphere at 42-63ms post-stimulus onset and repetition suppression within the left hemisphere at 165-215ms. The position-linked representation was characterized by a modulation within the left hemisphere at 20-39ms and at 143-162ms post-stimulus onset.

Within position-linked representations, the repetition-induced plasticity obtained with spatially-congruent pairs consisted of repetition suppression, whereas the repetition-induced plasticity obtained with spatially-incongruent pair consisted of repetition enhancement. Within these representations the repetition-induced plasticity consists of repetition enhancement solely when there is a spatial change across the different manifestations of the sound object. This is a first description of position-linked representations of sound objects and underlines the ecological importance of the issue.

In the last part of my work, I presented a first demonstration of repetition suppression for the motor output of the left hand associated with the presentation of environmental sounds related to manual actions. Repetition-induced plasticity occurred within the motor representations of action sounds located within the right hemisphere and influenced the excitability of motoneurons. Although the precise location of the neural population which is at the origin of this modulation is unknown, we presume an implication of the mirror neuron system, which has been described in human prefrontal and premotor cortex. Our study demonstrates that this link is characterized by repetition suppression, as most parts of semantic representations of environmental sounds. Our results predict that lesions of the motor cortex be associated with impaired recognition of action sounds; currently there is only circumstantial evidence from an association between limb apraxia and action sound recognition.

This works investigated the representations of sound objects in time, space and action which underlie the perception of sound objects. These representations are plastic as they are modulated by the experience of the listener and thus keep track of some information for a variable period of time. Further investigations should help to clarify the impact of several factors on sound object representations such as longer lag delays, spatial changes in the vertical plan, emotion perception, social situation or lesion of the primary motor cortex.

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